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COMMUNICABILITY OF LEPROSY AND APPLICATION OF CONTROL MEASURES

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It is interesting to observe the trend of opinion on the communicability of leprosy. The accounts of leprosy in the Bible leave one in no doubt that the ancient Jews believed that the disease was conveyed from person to person. The Biblical texts illustrate that this transmission ordinarily was considered as by natural means, but supernatural transfer is clearly indicated in the story of Naaman, whose leprosy was communicated to Gehazi through the curse pronounced by Elisha as a just punishment for avarice.[1] Nor do the drastic measures of isolation aimed at lepers during the middle ages leave any doubt as to how the people of that day felt on the subject of communicability. Then came a period in which communicability was thought to be a matter of little or no importance. Not long after the middle of the last century a distinguished medical body in England pronounced against the danger of transmission from person to person. After Hansen's discovery of the presence of the probably causative organism there came a general acceptance of the communicability of the disease. This view better than any other explains the observed and well established facts relating to leprosy. One might expect that the matter could be settled rather definitely by direct experimental evidence, but this type of evidence, if anything, serves to increase the obscurity surrounding the transmission of the disease.

All the experiments on laboratory animals may be dismissed because none of these animals has been found to be susceptible to infection with human leprosy.

There have been many purposeful attempts to transmit the disease from patients with active leprosy to other human beings by inoculation, but with the single, possibly successful, experiment carried out by Arning [2] in Hawaii, all the results have been negative. On the contrary,

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Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 3, 1937.

1. II Kings, 5.

2. Arning, E.: Verhandl. d. deutsch. dermat. Gesellsch. **1**:9, 1889.

there are a few apparently well authenticated examples of accidental transmission from person to person, and there is a modest number of cases of the infection of a physician, a priest or a nursing attendant connected with an institution in which lepers are cared for.

One of the first problems confronting the student of infectious diseases relates to the incidence of infection in any given community. Today this information is available in accurate form for only one place in the world. There are good data on the incidence of leprosy for the municipality of Cordoba on Mactan Island in Cebú, P. I., thanks to the careful studies Doull and his associates [3] made in 1933. He found that 1.72 per cent of the population of that municipality had recognizable manifestations of leprosy—this among a population of 6,063. It must be emphasized that this figure holds only for that particular community and for that time; it would not necessarily hold even for any other point in the Philippines. One of the interesting questions in this connection is what might be considered the "maximum susceptibility" of persons. Information is meager, but it is known from observations made in Hawaii that about 5 per cent of adults, either male or female, living with lepers in the marital relation contract the infection. This, it must be emphasized, holds only for Hawaii, since elsewhere in the world there are points where the incidence of susceptibility is much higher.

Whether race is a factor in susceptibility is a debatable question. It is often said that brown-skinned peoples are more susceptible to the disease than are others, but, so far as I know, there is no really substantial evidence on this point if all the factors in connection with the exposure are considered.

Boyd and Fox [4] stated the opinion that in Galveston, Texas, there was an undue incidence among American children of German-born parents. Obviously, there may always be better opportunities for exposure to the infection in a particular racial group.

In recent years it has become rather the vogue to consider susceptibility to leprosy to be greater in the early years of life. It is known that the highest incidence of the developed disease is in the second and the third decade, but, given sufficient opportunities for exposure, there is no question but that adults are infectible. There have been enough cases in which the disease developed in adults after a sojourn in countries where leprosy prevails to make this point clear.

The matter of transmission within the family is naturally most important. The doctrine of familial infection finds authority in the Bible, when David [5] pronounced a curse on Joab in these words: "Let

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3. Doull, J. A.; Rodriguez, J. N.; Guinto, R., and Plantilla, F. C.: Internat. J. Leprosy **4**:141, 1936.

4. Boyd, M. F., and Fox, W. F.: Pub. Health Rep. **35**:51 (Dec. 17) 1920.

5. II Samuel 3:29.

there not fail from the house of Joab one that hath an issue, or that is a leper." In Hawaii in 1914 among 1,060 lepers approximately 30 per cent had apparently been infected within the family circle. Doull and his associates in their much more recent study in the Philippines, found 27 of 104 lepers who apparently had been infected within the family group, making 26 per cent. In each of the communities referred to leprosy was sufficiently prevalent in the community as a whole to make it impossible to prove that the infecting contacts were not from some source other than the members of the family, although it is reasonable to assume that the infections were really contracted from within the family.

Related to the question of familial infection is that of house infection. Rogers [6] stated that probably 80 per cent of infections are due to living in the same house with lepers. This doctrine of house infection (though not in the sense Rogers intended) has at least the merit of an old and good foundation, for in the Bible [7] is found the following passage: "When ye are come into the land of Canaan, which I give to you for a possession, and I put the plague of leprosy in a house of the land in your possession . . ." This is followed by instructions as to what is to be done about the infected house; a reading of the full text makes it clear that the house itself was regarded as the source of the leprosy. Obviously, ordinary house infection is closely related to familial infection.

Much has been said about predisposition as an important factor in acquiring the disease; it has been only during the last couple of decades that anything accurate and helpful has been learned about individual predisposition to any infectious disease, and so far as leprosy is concerned students are in the dark. In recent years, with the rapidly increasing interest in nutrition as a factor in predisposing to infectious diseases, the suggestion has been made that diet is of importance in leprosy. No one today can either affirm or deny this, but it is certain that leprosy develops often in persons in an excellent state of nutrition.

Some authorities have held certain other communicable diseases as predisposing to leprotic infection; there is no substantial evidence for this point of view. Ordinarily it is customary to think of leprosy as being acquired by those living in poor sanitary surroundings, but enough exceptions to this rule have come to attention to make it doubtful that this is of any great importance.

The evidence available indicates that the nodular type of leprosy is more communicable than the neural type.

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6. Rogers, L.: Internat. J. Leprosy **4**:469, 1936.

7. Leviticus 14:34.

It is a customary statement in textbooks that prolonged and intimate contact is necessary for the transmission of the disease; this may be (and doubtless is) true in the majority of cases, but there are so many cases in which no contact, prolonged or otherwise, is to be discovered that one may wonder just how valid this statement may be.

One of the most remarkable of the features of leprosy, which apparently has some relation to communicability or perhaps to susceptibility, is to be found in the fact that nearly everywhere among adults there is a marked preponderance in the number of male lepers over that of female lepers; for example, the surveys in Hawaii have shown in the period from 1900 to 1913 that 35.5 per cent of cases were among female patients; a survey made by Wayson and Rhea [8] in the same community in 1933 showed about 40 per cent. In the survey of Doull and his co-workers in the Philippines the figures showed approximately two males to one female.

To my mind the most interesting, and I suspect the most significant, factor in the communicability of leprosy is the geographic distribution of infectiveness. Many examples of what I have in mind might be cited from abroad, but I can best illustrate my point by the evidence available in this country. In the United States there are three types of communities with respect to communicability of leprosy: first, the areas bordering on the Gulf of Mexico, especially parts of Florida, Louisiana and Texas, in which the disease spreads relatively freely; second, certain southern and western communities, especially parts of Florida, Georgia and South Carolina, in which it spreads relatively feebly, cases occurring at intervals of years, apparently barely enough infection being present to keep the disease alive, and third, the remainder of the country, especially the large metropolitan areas, in which, for practical purposes, the disease does not spread at all. This is well illustrated by the experience in the Northwestern states. Approximately two hundred Scandinavian lepers became residents of Minnesota and adjacent states in the latter half of the past century, and from these the disease developed among a few of their descendants who were born in this country and the persons with whom they came in contact. In other words, in this area the definite tendency of the disease was to die out rather than to spread. This is markedly in contrast with observations in communities in the first category I mentioned. One's first mental response to these facts is that the determining factor is climatic, but this is speedily seen to be an inadequate explanation. While it is true that leprosy is more prevalent in warm lands than in cold ones, yet in the Scandinavian

8. Wayson, N. E., and Rhea, T. R.: Leprosy: Observations on Its Epidemiology in Hawaii, Public Health Bulletin 212, United States Treasury Department, Public Health Service, 1934.

countries the disease has been prevalent to a serious extent during the past century; in the latter part of the last century a definite though limited outbreak occurred in the Memel district of what was then East Prussia, and Iceland once had many lepers and even now has a few. Hence, some influence other than climate must be operative. There is no adequate explanation for this curious geographic localization of infectivity, but it is of great practical importance.

The exact mode of transmission of the disease is unknown, and because of that its spread has been attributed to direct contact with patients in whom the disease has developed, with persons in whom it is latent and even with possible carriers. I realize that one is treading on uncertain ground in referring to patients with "latent" leprosy and to "possible carriers" as sources of infection, but it seems necessary to assume the existence of these to account for the appearance of the disease in communities in which a long interval has elapsed since its last appearance and in which there is no recognizable association between the appearances. At present, however, such possible sources of infection serve as nothing more than interesting subjects of speculation.

Now I shall turn my attention for a moment to control measures. This is an unsatisfactory subject for discussion, because evidence of the efficiency of such measures is by no means clear. Until comparatively recently control, when practiced at all, resolved itself into segregation of the afflicted persons. In a few cases this meant confining the patient to his own domicile and taking such other precautions as seemed indicated. This method has never found official favor in the United States or in any of the countries subject to the jurisdiction of the United States. A second type of segregation, i. e., institutional, has been preferred, and this is generally most stringently enforced where it is least needed—another way of saying that communities in which leprosy is not a real menace are much more likely to, shall I say, "inflict" rigorous segregation than are communities in which the disease is common and shows a definite tendency to spread. In any event, so far as I know, there is no real proof of the efficiency of segregation as a measure for public health; one cannot make out a convincing case for it on those grounds. From the point of view of the esthetic interests of a community and from that of public charity, it is readily justifiable.

It is proper to ask why segregation, which has been practiced so long and so rigorously in some places, has not given a better account of itself. Here are some of the difficulties encountered: First, there is the long period of incubation, or "latent" period, averaging from six to eight years, and, in several cases with which I am acquainted, it has been longer than fifteen years; it is possible that during a part of this long period of development the disease is in a communicable stage. Second, there is the difficulty of early diagnosis, even after the infection

has progressed to the stage of being a recognizable clinical entity. The difficulty is not so much that the physician fails to arrive at a correct diagnosis (though often that difficulty is real enough); rather it is in getting the patient to go to the physician early, on account of the relatively insignificant early manifestations of the disease, which disturb the patient little or not at all, and of course sometimes there is wilful concealment. Third, there are the inherent difficulties of segregation, the expense, which is prohibitive for communities where the disease is prevalent; the social and economic handicaps on families and, finally, the difficulty of keeping patients in confinement in an institution.

Soon after the American occupation of the Philippine Islands a great deal was heard about the attempt to eradicate leprosy from the islands. It was to be done by means of vigorous measures to be taken by the American government. The vigorous measures were, and still are, taken, and the Philippine medical authorities are still arguing about their efficiency, as there is no substantial evidence that the measures have reduced the number of lepers in the islands.

Whether the marked decrease in leprosy which has occurred in Hawaii during the past few decades is attributable to the thorough and intelligent application of segregation cannot be definitely ascertained; there are many factors in addition to segregation which need to be considered. Holding, as I do, the view that geographic location is the factor determining whether a leper is a menace to those with whom he comes in contact, I feel that control measures need to be applied with much discrimination and that much latitude should be allowed to public health authorities. In communities in which the disease shows a definite tendency to spread, lepers should be isolated as promptly as possible, preferably in an institution and in the home in exceptional cases. In communities in which it is known that propagation is impossible, segregation may be left to the option of the patient and his medical adviser; often it is necessary on account of social and economic factors. In communities in which experience has shown that the tendency to spread is feeble I should suggest that each case be considered from the point of view of risk of transmission of the infection. A patient with ulcerating nodular leprosy would be segregated, while one with neural involvement alone would be left at liberty.

Even in areas in which communicability of the disease is established I should be lenient in the release of patients with arrested manifestations. I am disposed to feel that the clinical condition of the patient, rather than the results of microscopic examination, should govern in such cases. Back of this inclination on my part to be lenient on the whole subject of control of the disease lies my feeling that in any community the disease runs a course largely independent of attempts hitherto made to control it.

LEPROSY

A REVIEW OF SOME OF ITS UNUSUAL FEATURES

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The diagnosis of advanced leprosy presents no difficulty; the organisms are found readily, and the characteristic histologic changes are present in some lesions. Bizarre manifestations are occasionally seen but usually do not obscure the typical clinical picture. However, when such manifestations assume a major role and no classic signs are present, the clinician is apt to be misled. Such an instance was Pardo-Castello's case of dermatitis atrophicans diffusa et progressiva,[1] which could easily have been passed as having no connection with leprosy by clinicians less astute in the diagnosis than he.

The disease may begin in an unusual manner, develop insidiously and parade for some time unrecognized. Ayres[2] reported a case with such a background before the Los Angeles Dermatological Society in 1935. His patient showed a thinning of the right eyebrow, diffuse flushing of the face and tissue-paper-like atrophy of the skin of the hands, the arms, the feet and the legs. Bacilli were found in the tissue. The patient for five months had passed through clinics for the treatment of allergy, of diseases of eye, ear, nose and throat and of cutaneous diseases with diagnoses of allergic eczema, acne and rhinitis.

Again, the clinical evidence may be convincing, but the diagnosis is difficult to confirm either because bacilli cannot be found or because the histologic picture is not definite. The following reports illustrate this:

In 1930 Finnerud[3] presented the case of an 18 year old Filipino who had an eruption of seven months' duration that was clinically suggestive of leprosy, but no bacilli were obtained and the histologic picture was not characteristic. This eruption was generalized, with discrete papular and nodular lesions. There was an infiltrated, reddish scaling plaque involving the major portion of the left buttock, part

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1. Pardo-Castello, V.: Leprosy Associated with Dermatitis Atrophicans Diffusa et Progressiva, Arch. Dermat. & Syph. **33**:12 (Jan.) 1936.

2. Ayres, Samuel, Jr.: Leprosy, Arch. Dermat. & Syph. **33**:769 (April) 1936.

3. Finnerud, C. W.: A Case for Diagnosis, Arch. Dermat. & Syph. **22**:339 (Aug.) 1930.

of its center being less infiltrated and possibly clearing. A patch on the buttock was anesthetic. At the same meeting Becker [4] presented a case in which a plaque involved the median portion of the cheeks, the upper lip and the eyelids. Histologic examination showed tubercles and an infiltrate of epithelioid and lymphocytic cells but no caseation or acid-fast bacilli. In the discussion of these two cases Dr. Becker remarked on the difficulty of finding the organisms in a sarcoid type of leprosy; Dr. H. E. Michelson suggested producing a shock in an effort to set free the organisms, and Dr. M. H. Ebert expressed the belief that the organisms were destroyed rapidly and that there was a high state of cutaneous sensitivity.

In 1930 Wile [5] presented before the Chicago Dermatological Society a Chinese who had a maculo-anesthetic lesion of one year's duration on his neck and face. Its center resembled morphea, and the borders were hypersensitive. The ulnar nerves were mildly enlarged. Histologic examination showed a chronic infectious granuloma with Langerhans cells. No bacilli were found in nasal smears or in biopsy material. The finding of numerous giant cells and no bacilli caused the pathologist to lean toward the diagnosis of tuberculosis. The diagnosis of leprosy was concurred in by the discussers.

Stillians [6] in 1931 presented a Mexican laborer who had an oval, sharply defined plaque of three years' duration near the angle of the jaw, another on the end of the left brow and one on the left leg near the ankle. The lesions showed atrophy, annular configuration and anesthesia. No organisms were found. Ebert, in discussing this case, mentioned an experience with a case of clinically established leprosy in which bacilli were readily found; previously, during a long period of observation in the hospital, search for bacilli had been futile.

Similar instances have been reported by Lunsford,[7] Jacobson,[8] Cornbleet and Pace [9] and Combes.[10]

Such experiences are probably frequent in countries where the disease is common. The clinical diagnosis is better fortified in such

4. Becker, S. W.: A Case for Diagnosis, Arch. Dermat. & Syph. **22**:340 (Aug.) 1930.

5. Wile, U. J.: Hansen's Disease, Arch. Dermat. & Syph. **24**:516 (Sept.) 1931.

6. Stillians, A. W.: Leprosy, Arch. Dermat. & Syph. **25**:168 (Jan.) 1932.

7. Lunsford, C. J.: Urticaria Pigmentosa, Arch. Dermat. & Syph. **23**:397 (Feb.) 1931.

8. Jacobson, H. P.: Lupus Erythematosus, Arch. Dermat. & Syph. **28**:911 (Dec.) 1933.

9. Cornbleet, T., and Pace, E. R.: Scleroderma, Arch. Dermat. & Syph. **30**:132 (Jan.) 1934.

10. Combes, F. C.: A Case for Diagnosis, Arch. Dermat. & Syph. **29**:312 (Aug.) 1934.

countries because of the high incidence of the disease; but in the United States diagnosis on clinical grounds without laboratory confirmation is extremely bold, unless the picture is classic.

In the past fifteen years I have accumulated a few cases which illustrate the fact that the premonitory signs of a typical clinical picture may be present a long time before the patient is aware of them or the physician recognizes their true nature and, therefore, that the period of incubation may not be as long as is commonly supposed.

With these cases this report includes a group in which the period of incubation can be approximated and a brief review of recent literature on therapy.

It is hoped that such a report will stimulate further interest in the broader aspects of the disease and thereby help in earlier diagnoses.

EARLY LEPROSY

REPORT OF CASES

CASE 1.—A white man aged 23 was first seen in 1922. He had been born and reared in Texas. In 1917 both feet had been frost bitten. In 1920 a callus formed on the ball of the right foot. It had not been present long before the right inguinal glands enlarged and became tender. The callus broke down soon into a perforating ulcer. In 1921 it was curetted, and necrotic tendons were removed. At the same time the surgeon removed four enlarged inguinal lymph glands. Healing ensued after three months had been spent in bed. Two months after the patient began walking on the foot again ulcus perforans recurred.

When the patient was seen by me there was a dry oval ulcer 0.5 cm. in diameter and in depth, with a surrounding ring, about 8 mm. wide, of dense hyperkeratosis. The patient was observed for two months. No etiologic diagnosis was made.

He was not seen again until 1927 (five years later), when he presented advanced cutaneous leprosy, various-sized nodules being present on the face, the body and the extremities. The ulnar and the peroneal nerves, particularly the right peroneal nerve which had nodulations along its course, were perceptibly enlarged.

The patient stated that in the latter part of 1922 the head of the right first metatarsal bone had been removed, and after one year had been spent in bed healing occurred. In 1923 the Wassermann reaction was found to be positive, and during the next one and a half years the patient received fifty injections of neoarsphenamine. About three months after receiving his last antisyphilitic treatment (1925) he noticed small nodules appearing on the upper part of his back and the left thigh. They gradually increased in size and became widespread and thickly set over his face, neck, extremities and body. He had complained of "catarrh" for the previous three years, and two years before (when he had nodules on his face) submucous resection had been performed.

When seen by me in 1922 his serologic reaction was negative. No examination of the spinal fluid was performed, and no studies of tissue were made. There was no record of palpating the superficial nerves or of examination for anesthesia. However, the patient stated in 1927 that both feet had felt "numb" for years. There was no eruption on his body in 1922, at which time he appeared to be in

good general condition. It is conjectural but reasonable to suppose that this perforating ulcer was due to leprosy which remained dormant for five years, as the neural type.

CASE 2.—A man 39 years old was first seen in July 1922, when he presented above the inner condyle of the left humerus an oval lesion about 10 cm. in longitudinal diameter (fig. 1). Its periphery was light red and about 0.5 cm. wide, fading into the normal skin. Its center was a dirty chamois or yellowish color. Below, on the forearms, were two small macules of the same color. There was no scaling or atrophy in the lesions. Leprosy was suspected. The serologic findings were negative. Two nasal smears showed no acid-fast bacilli. Serum from the lesion on the arm was stained for bacilli, but none were observed. There was no change in thermal or epicritic sensibility or in the perception of pricking.

Fig. 1 (case 2).—First sign of the disease, four years before a definite diagnosis was made.

Two years later the patient was examined. A small bean-sized nodule was removed from his back. Its histologic picture was that of inflammatory granuloma with epithelioid infiltration in a loose reticulum in the papillary and deeper layers of the cutis. There were no giant cells. Again no bacilli could be found in the lesion or in nasal smears. The macular lesion on the arm persisted with no change.

The diagnosis of leprosy could not be confirmed.

Two years later (four years after the onset of the original lesion) the patient presented typical nodular leprosy, and organisms were readily found.

Another case of early leprosy is interesting from the standpoint of mimicry:

CASE 3.—An unmarried woman, aged 25, presented "ringworm on the forehead." Above the right eyebrow was a scaling red raised plaque, which was edematous and inflamed from the use of strong medication. A single raised lesion in this location aroused the suspicion of syphilis. The lesion had been present four months and was not enlarging. Examination revealed another lesion just above the outer malleolus of the right ankle (fig. 2), from which the diagnosis was made. This was oval and about 8 cm. in its greatest diameter. It had an irregular slightly raised border of a light brown or copper color and was slightly scaly and dry, with pronounced cross-hatching, resembling the mosaic appearance of lichen planus. Leprosy was suspected for the following reasons: There was no itching, as in lichen planus or circumscribed neuro-

Fig. 2 (case 3).—Interfollicular cutaneous leprosy at the outer malleolus of the foot.

dermatitis; the lesion was anesthetic; histologic examination showed superficial interfollicular granuloma in the papillary and the subpapillary layer, with foam cells, epithelioid cells and occasional giant cells; acid-fast bacilli were observed with the Ziehl-Neelsen stain.

The interfollicular type of lesion was clearly described by Rogers and Muir.[11] Those authors classified cutaneous leprosy as that form in which the bacilli are present in such quantities that they can be found on bacteriologic examination. They listed three subtypes: (1)

11. Rogers, Leonard, and Muir, Ernest: Leprosy, Bristol, John Wright & Sons, Ltd., 1925, p. 189.

papillary, (2) interfollicular and (3) subfollicular, the classification being made according to whether the infection is limited to the papillary layer of the corium, has spread to the region between the follicles or has reached the region deeper than the follicles.

They state that

> in the interfollicular sub-type the bacillary infection, and consequent edema, is in the layer of the corium between the hair follicles [fig. 3]. The clinical appearance is typical, and resembles the mosaic arrangement found in lichen planus. The

Fig. 3.—Section of the interfollicular lesion of cutaneous leprosy.

> natural folds of the skin are exaggerated and deeper than normal, and the areas between these folds stand out in relief. This is due to the upward pressure exerted by the edematous and granulomatous swelling of the corium, the tension being resisted by the hair follicles and sweat ducts, which pull the epithelium and thus exaggerate the natural folds of the skin.

BULLAE IN LEPROSY AND FEBRILE ATTACKS

The best example in recent literature of the assumption by a bizarre manifestation of such a predominant role that the true nature of the disease is masked is in the description of Lazarine leprosy by Pardo-

Castello,[12] in which the early and only signs are bullae, subsequent ulcerations and universal atrophy.

Cottini [13] expressed the belief that febrile erythema and erythema multiforme are of possible leprous nature in Cuba, as often, he said, the first manifestation of leprosy is an attack of erythema multiforme with nodular lesions.

The development of bullae in the course of the disease (when not the result of trauma to an anesthetic part) is uncommon and is apt to mislead the observer, because it is not a part of the classic picture. Chevarria and Barrera [14] stated that pemphigus is a frequent manifestation of early neural leprosy. Jeanselme and Horowitz [15] reported a case of the disease in which there were a vesiculobullous eruption that resembled Duhring's disease and malaria, and microfilaria of Bankroft were found in the blood. Oliver and Finnerud [16] presented a case of classic leprosy in which there were a few bullous lesions.

I had the opportunity to follow a case of nodular leprosy during three attacks of leprotic fever. In each exacerbation there were fresh lesions, many of which appeared as erythema multiforme, and bullae formed on the erythematous lesions. The acute eruption overshadowed the picture of leprosy. Synchronously there was an acute inflammatory reaction in the nodules. The febrile reaction lasted for from one to two weeks. As the bullae subsided they dried, leaving a violaceous and brawny pigmentation which gradually faded to normal.

The febrile reaction commonly has been initiated by an intramuscular injection of ethyl chaulmoograte. Occasionally the oil leaves more or less painful lumps at the sites of injection. When an injection is given in the neighborhood of this induration it is likely to be followed by a febrile attack. This occurrence has been so common that I have become wary of continuing the injections in cases in which a lump from a previous injection is present. In one case all the nodules softened during the febrile stage, and many became cold abscesses. As the acute reaction subsided thin pus drained from these, and they dried up and shrank.

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12. Pardo-Castello, V., and Caballero, G. M.: Lazarine Leprosy: A Peculiar Monosymptomatic Form of Leprosy, Arch. Dermat. & Syph. **23**:1 (Jan.) 1931.

13. Cottini, G. B.: Three Cases of Leprosy, with Special Reference to Bacillemia, Gior. ital. di dermat. e sif. **74**:84 (Feb.) 1933.

14. Chevarria, A. P., and Barrera, F. de P.: Arch. y rev. de hosp., Havana, October 1936.

15. Jeanselme, E., and Horowitz: Unusual Pruriginous Leprosy in a Patient with Malaria and Microfilariasis, Bull. Soc. franç. de dermat. et syph. **35**:538, 1928.

16. Oliver, E. A., and Finnerud, C. W.: Hansen's Disease, Arch. Dermat. & Syph. **20**:379 (Sept.) 1929.

The aforementioned development of bullae and abscesses in the febrile stage is a part of what Rogers and Muir described as elimination phenomena. They stated that there is strong bacteriologic and clinical evidence that immunity may be acquired and cite the elimination phenomena as such evidence. These are:

> (1) The gradual arrest of the progress of a severe and prolonged reaction even though, towards the end of it, the patient is so weak and exhausted that one would expect that that would be the time when . . . bacilli would . . . multiply rapidly, and invade and swamp the devitalized human organism. (2) The gradual breaking down and granulation of bacilli, which take place spontaneously or occur more rapidly as the result either of treatment or of some intercurrent disease. (3) The characteristic appearances of skin lesions showing the signs of rapid resolution. (4) Rapid disappearance of inflammatory points, resulting from bacillary embolism, in the capillaries, caused by bacilli set free in the blood-stream from old lesions during reactions.

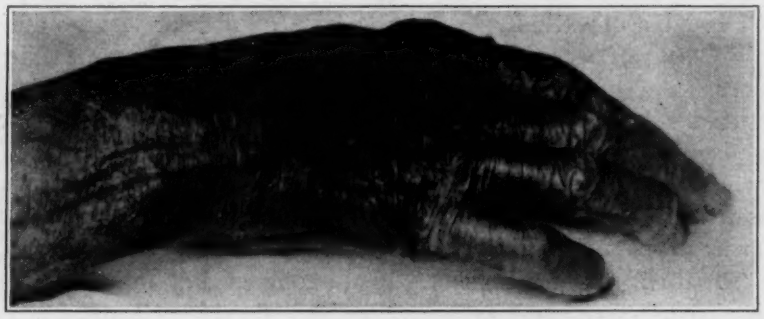

Fig. 4.—Atrophy following elimination phenomena.

Rogers and Muir called the stage at which the elimination phenomena are present the third stage of the disease, the first stage being that in which the bacilli are still few in the body and the second stage that in which the bacilli have multiplied and the disease is still spreading but in which the elimination phenomena have not yet appeared.

The fourth stage might well be the stage at which all elimination phenomena are finished and atrophy of the skin is the only sign of the disease. Areas of atrophy frequently mark the sites of large lepromatous plaques which have undergone one or more of the acute reactions that attend leprotic fever. The crinkled skin on the ear lobes and the loose skin of the hands (fig. 4) are illustrative of this. A rather peculiar picture is presented when these plaques of induration cover a wide area, such as the whole dorsal surface of the forearm. Such lesions when subacute are scaly, and the infiltration is deep in the cutis (fig. 5). During leprotic fever these become edematous and have a boggy feel. They may remain for a long while, but eventually resolution takes place, leaving atrophic skin.

PERIOD OF INCUBATION

The common idea is that the period of incubation is long. This is true in most instances. Various authors have estimated it to be from two to twenty years. Rogers and Muir estimated that it averaged between two and four years. Pierini [17] stated that among children of lepers 42 per cent of those who continued living at home acquired the disease in from three to six years, while only 0.5 per cent of those who were separated from their parents were afflicted.

Denney and Ritter [18] have intimated that leprosy, like tuberculosis, is more likely to be contracted in childhood than in adult life. Natural immunity, no doubt, is a factor which determines the onset of definite manifestations.

Fig. 5.—Large deeply indurated plaques.

I have had the opportunity of observing the disease in four families in which there was fairly continuous contact. Assuming that familial contact was the only source of infection, I may illustrate the variations in the period of incubation through this group:

FAMILY 1.—The presence of leprosy was established for the father, three sons and one grown daughter in 1907. These five persons were dead in 1923, when I visited the family. At this time there were two adult daughters and one son afflicted with cutaneous leprosy, the disease having appeared in them in late adolescence. One of the daughters, aged 25, had three children ranging in age up to 4 years, with no signs of the disease. The other daughter, aged 23, had a healthy-looking 3 year old child.

17. Pierini, L. E.: Prophylaxis of Leprosy in Early Childhood, Semana méd. **2**:988 (Oct. 3) 1929.

18. Denney, O. E., and Ritter, J.: The Noticeable Parallelism, the Apparent Similarity and Close Resemblance Between the Two Chronic Diseases, Tuberculosis and Leprosy, Illinois M. J. **49**:318 (April) 1926.

FAMILY 2.—A girl was first seen in 1922, at the age of 20, with neural leprosy. In the course of ten years the condition changed to a diffuse nodular type. Her first manifestation was noted about the age of 18. She played with the girls in family 1 during childhood.

FAMILY 3.—Two sisters, aged 30 and 35, were cousins of the girl in family 2. One presented neural leprosy and the other the cutaneous type (one nodule on the back, which showed a characteristic histologic picture and the organisms). The manifestation had appeared gradually in the first patient in adult life. The other patient was not aware of any cutaneous lesion.

FAMILY 4.—An aunt of the girls in families 2 and 3, in whose home they spent much time in childhood, was seen in 1936 at the age of 60, when she presented an erythematous blotch on the right jaw, which was roughly circular, slightly raised and edematous and looked like erysipeloid; a red puffiness of the lobule of the right ear, and two scaly bronzed lesions, one over the promontory of the seventh cervical vertebra and one on the left wrist. She recently suffered a febrile attack, with new lesions appearing as erythema nodosum on the face, the body and the extremities. The superficial nerves have been painful.

Approximating the time of infection between these contacts, I should estimate the periods of incubation in this series to be as follows: in family 1, from five to ten years; in family 2 from eight to ten years; in family 3, from fifteen to twenty years, and in family 4, from twenty to twenty-five years. My impression from observing this group of cases is that the older the person is when infected, the longer will be the period of incubation.

Cases 1, 2 and 3 and the case of the younger sister in family 3 illustrate well that the patient's story of the original development of the disease may not be reliable and therefore cannot always be a basis for computing the period of incubation. In cases 1 and 2 the diagnosis was not possible until five and four years, respectively, after the appearance of the initial signs. One of the girls in family 3 would not have known of her infection as early as she did, had she not been aware of its presence in her sister and submitted herself to inspection.

HISTOPATHOLOGIC PICTURE

I have examined some of the large indurated plaques microscopically in the subacute stage. Bacilli were difficult to find. The epidermis showed few rete pegs and was thinner than normal. The infiltration in the cutis was a loose arrangement of epithelioid and plasma cells. Few foam cells and no giant cells were seen. The most outstanding feature was a pronounced fibroblastic reaction throughout the cutis. The lymph and blood spaces were dilated, as would be expected. There was not the true lepromatous arrangement of the infiltrate, in which inflammatory cells mantle the vessels and the glands.

Another section was taken from a plaque which formed at the site of a maculo-anesthetic lesion over the seventh cervical vertebra during an attack of leprotic fever (fig. 6). This lesion, which previously was

anesthetic, copper colored, scaly and not indurated at all, covered an oval area about 4 cm. in diameter. This and other lesions became raised, red and edematous, giving the appearance of generalized erythema multiforme. The fibroblastic reaction was evident in this tissue. The cellular infiltrate was made up of epithelioid and plasma cells and a few foamy cells, and fibroblasts were seen attempting to separate the infiltrate into clumps (a picture of sarcoid).

The fibroblastic reaction in the subacute plaque and the same reaction in a slightly different induration were attended with sparse bacilli. It is commonly known that the sarcoid or tuberculoid lesion contains few bacilli. It seems to me, therefore, that whenever the reaction of the

Fig. 6 (family 4).—Section showing sarcoid structure.

tissue is fibroblastic there is a coincident destruction of bacilli (or a mutation of them), rendering search for them almost futile.

SEARCH FOR BACILLI

The means of early diagnosis are bacteriologic and histologic. The Rubino test (with sheep cells and solution of formaldehyde in saline solution plus human serum), discussed by Monacelli,[19] and other specific tests for leprosy have not been used widely enough to be trustworthy. True lepromas are not seen early (case 3 is an exception), as would be expected from the fact that the disease has a strong predilection

19. Monacelli, M.: The Rubino Reaction in Leprosy, Gior. ital. di dermat. e sif. **69**:1472 (Oct.) 1928.

for nerve tissue, settles there first and commonly gives rise to signs or symptoms only of neural leprosy for a long time. Indeed, in a case in which numerous oval lesions of various sizes with raised scaly pigmented borders and lighter-colored centers had been present over the body for five years and in which there was a nasal perforation from a previous involvement, there were no characteristic histologic changes. There was dense fibrosis in the cutis, with an occasional giant cell and a pseudotubercle. No bacilli were found in the tissue or on nasal smears. The patient was admitted at the United States Marine Hospital, Carville, La., on clinical grounds alone.

The incidence of bacilli in nasal smears in Rogers' and Muir's experience was 37 per cent in 206 cases of cutaneous (nodular) and mixed infection and 3.8 per cent in 103 cases of neural leprosy. Of cases which I have observed, there were positive nasal smears in 35 of 37 of cutaneous involvement and in only 2 of 7 of neural involvement. Unless the turbinates are enlarged or nasal blockage is present, the nasal smears are likely to show no bacilli. Occasionally it is worth while to anesthetize the nose and curet for a specimen. However, a leproma in a turbinate is rather easily abraded with firm pressure of a cotton swab, and this method of obtaining a specimen is usually satisfactory. The bacilli may be found occasionally in scrapings of epithelial cells (Muir and Chatterji [20]) or in serum from a punctured nodule. In the case in family 4 they were found only in serum collected from the lobule of the ear after bleeding from several punctures stopped. Even during a febrile attack in this case the search in tissue and nasal smears did not reveal bacilli any more readily than before. Stein and Steperin [21] were able to show that bacilli may be present in the normal skin of a leper in areas that have never been the sites of lesions. They examine fluid from the tissues, obtained by superficial incision with a scalpel, and the contents of vesicles produced by freezing with solid carbon dioxide.

Serra [22] has found the bacillus in the lymph extracted from the lymphatic glands of the groin, the neck, the axillae and other locations in practically all cases of leprosy. Hansen's bacilli were found in the lymphatic glands of apparently healthy persons who were in daily contact with lepers. The bacillus was isolated in the blood of 3 of 33 patients examined.

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20. Muir, E., and Chatterji, S. N.: The Infection of Stratified Epithelium in Leprosy, Indian J. M. Research **19**:1163 (April) 1932.

21. Stein, A. A., and Steperin, M. I.: Excretion of Lepra Bacilli by Lepers, Urol. & Cutan. Rev. **38**:776 (Nov.) 1934.

22. Serra, A.: Biologic Researches on the Leprous Infection, Gior. ital. di dermat. e sif. **67**:1109 (Aug.) 1926.

Other methods mentioned by various authors for finding the bacilli have been: freezing the skin and examining the fluid from vesicles and producing a leprotic fever with potassium iodide.

Lowe [23] advised staining tissue for bacilli with a special method which requires little alcohol, so as not to decolorize the bacilli, a distinct advantage, particularly in tissue in which the bacilli are sparse. In a recent case Lowe's stain showed the organisms about the sweat glands much more definitely than did the Ziehl-Neelsen stain.

In cases in which leprosy is suspected but in which the histologic picture is not pathognomonic and bacilli cannot be found, great importance has to be attached to the clinical signs. Since it is not uncommon for the disease to appear in a bizarre manner or to mimic other conditions and parade masked for a long time before giving rise to a more nearly classic picture, one's diagnostic acumen has to be kept sharp to recognize it. Such acuteness is no doubt prevalent among physicians in the South, where the disease is more frequently met.

TREATMENT

Besides chaulmoogra oil and its derivatives, other drugs are mentioned in the literature with more or less favor.

Sézary, Dérot and Guédé,[24] basing their therapeutic attempt on the apparent relation of Mycobacterium tuberculosis to Bacillus leprae, employed gold salts in three cases. One patient seemed to be temporarily benefited; the other two became worse.

Paldrock's [25] treatment consists essentially of freezing lesions every two weeks for from three to four seconds with solid carbon dioxide. This, he stated, results in auto-immunization, with an improvement in the untreated as well as in the treated lesions. The treatment is continued for four months, after which a series of injections of a gold compound is given. Patients have remained clinically and bacteriologically cured for as long as five years. General systemic treatment is carried out in conjunction with the specific routine, nourishment and exercise being stressed. Jaja [26] reported good results with the use of sodium gold thiosulfate.

Stein [27] gave to a series of patients from 1 to 5 cc. of a 1 per cent solution of antimony and potassium tartrate every two days. The use-

23. Lowe, John: A Note on the Staining of Mycobacterium Leprae in Tissue Sections, Indian J. M. Research **22**:313 (Oct.) 1934.

24. Sézary, A.; Dérot, M., and Guédé, M.: The Treatment of Leprosy with Gold Salts, Bull. Soc. franç. de dermat. et syph. **36**:1071 (Nov.) 1929.

25. Paldrock, A.: A Specific Method in Treatment for Leprosy, Dermat. Wchnschr. **92**:273 (Feb. 21) 1931.

26. Jaja, G.: Aurotherapy of Cutaneous Tuberculosis, of Leprosy and of Psoriasis, Gior. ital. di dermat. e sif. **69**:846 (June) 1928.

27. Stein, A. A.: Treatment of Leprosy, Dermat. Ztschr. **63**:393 (May) 1932.

fulness of that treatment was found to be limited to acute exacerbations of the condition, which it apparently controlled in a satisfactory manner. It was useless in the stationary stage and did not protect against the development of new exacerbations. Cochrane [28] mentioned the use of from 0.02 to 0.04 grain (0.0013 to 0.0026 Gm.) of antimony and potassium tartrate in 4 cc. of distilled water intravenously every other day. He stated that it controls leprotic fever most remarkably.

Throne [29] reported a remarkable improvement in a case of maculoanesthetic leprosy treated with a course of 0.06 Gm. of antimony arsphenamine each week combined with 5 minims (0.3 cc.) of chaulmoogra oil three times a day. He noted that the lesions disappeared; the interosseous spaces filled out; the interosseous muscles recovered their power, and the general condition improved. Kingsbury [30] reported in more detail concerning this treatment in 1931.

Paldrock and Pooman [31] noted that leprosy bacilli soaked in 10 per cent sodium thiosulfate were gram-negative after twenty-four hours. Furthermore, smears from freshly excised lepromas soaked in the same solution for twelve hours showed gram-negative organisms. These observations have encouraged the authors to treat leprosy with sodium thiosulfate.

Tomb,[32] in commenting on the employment of potassium iodide, stated that after its use reactions occur in which the nodules, as well as the thickened cutaneous lesions, become swollen and inflamed, while fresh crops of nodules appear. Fever accompanies this reaction. After it subsides the nodules are smaller, and the skin is thinner than before. As the leprotic foci are broken down, the bacilli are set free and appear in the blood and the nasal discharges. While such reactions are not desirable, in cases in which the organisms become negative after potassium iodide therapy relapse is less likely than in those in which the organisms become negative under treatment with chaulmoogra oil. Phipson [33] used this drug as a test for cure. Cochrane, commenting on fever therapy in the disease, advised it in the early stages and for proof

28. Cochrane, R. G.: A Review of the Present Methods of Treatment of Leprosy, Brit. J. Dermat. **42**:125 (March) 1930.

29. Throne, B.: Maculo-Anesthetic Leprosy, Arch. Dermat. & Syph. **17**:262 (Feb.) 1928.

30. Kingsbury, J.: A New Antimony Compound in the Treatment for Leprosy, Arch. Dermat. & Syph. **24**:1053 (Dec.) 1931.

31. Paldrock, A., and Pooman, A.: The Effect of Sodium Thiosulfate on the Organism of Leprosy, Dermat. Wchnschr. **98**:417 (April 7) 1934.

32. Tomb, J. W.: Chaulmoogra Oil and Its Derivatives in the Treatment of Leprosy, J. Trop. Med. **36**:170 (June 15); 186 (July 1) 1933.

33. Phipson, E. S.: Aden and Its Leprosy Problem, Leprosy Rev. **5**:4 (Jan.) 1934.

of cure in the late stages. He said that he starts its administration with ½ grain (0.03 Gm.) and increases the dose by 2 grains (0.13 Gm.) daily until 15 grains (0.97 Gm.) are taken; then the dose is doubled. When the dose has reached 30 grains (1.9 Gm.) the drug is given twice a week, increased gradually by 10 grains (0.65 Gm.) until 240 grains (15.7 Gm.) is administered in one dose. He recommended protein shock with milk and injection of typhoid vaccine for inducing fever.

Pinard, Rabut, Girand and Abricosoff [34] reported a case in which leprosy was undergoing fairly rapid evolution, despite treatment with chaulmoogra oil. Treatment by impaludism was employed. After seven febrile attacks the malarial infection spontaneously disappeared. There was definite but transitory improvement in the leprous lesions.

Gohar [35] treated a number of patients with a vaccine prepared from organisms recovered from leprotic nodules. He reported good results in nodular leprosy and doubtful ones when the condition was anesthetic. He mentioned previous work with specific vaccines by Devoto, Mariani, Hasson, Mastuda and Row as either prophylactic or therapeutic.

Audry and Viev [36] gave to a patient with nodular leprosy a vaccine of Ducrey bacilli (Dmelcos vaccine) every four days and produced violent congestion of the lesions on the face. Chaulmoogra oil was given at the same time. This combined treatment produced unusually rapid improvement in the eruption.

S. de Novaes e Silva [37] reported the use of tuberculin in three lepers, one of each type. There was no therapeutic effect in neural leprosy. He noted a cessation in the nasal discharge of one patient.

Roussel [38] has made several enthusiastic reports of his results with anthrax vaccine. Of 17 patients with neural leprosy 88 per cent are apparently well; 9 with the tubercular type were not benefited, and 1 with the mixed type is apparently well.

Ephedrine, ½ grain (0.03 Gm.) in a drachm (3.9 Gm.) of water, has been mentioned by Cochrane and by Phipson as being of good service in the relief of the neural pain, particularly in the febrile stages of the disease.

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34. Pinard, M.; Rabut; Girand, and Abricosoff: Leprosy Treated with Malaria Therapy, Bull. Soc. franç. de dermat. et syph. **36**:648 (July) 1929.

35. Gohar, M. A.: Vaccine Treatment of Leprosy, J. Trop. Med. **34**:166 (June 15) 1931.

36. Audry, C., and Viev: The Action of Anti-Chancroid Vaccine (Dmelcos) in a Case of Nodular Leprosy, Bull. Soc. franç. de dermat. et syph. **35**:430 (May) 1928.

37. de Novaes e Silva, S.: Tuberculin in the Treatment of Leprosy, Rev. méd.-cir. do Brazil **35**:83 (March) 1927.

38. Roussel, J. N.: A Report of Twenty-Seven Cases Treated with Anthrax Vaccine, J. Trop. Med. **38**:133 (June 1) 1935.

In 1933 Ryrie [39] reported on the use of several different dyes intravenously. His best results were apparently from trypan blue. I had the opportunity soon after his report to give this dye to a patient. When 5 cc. of a contemplated dose of 20 cc. were administered, the patient collapsed with respiratory failure, which was all but followed by cardiac failure. He was revived in a few minutes, which seemed like hours. The condition was moderately advanced; there were occasional febrile reactions and gradually increasing weakness. After the injection of dye he became further weakened, and it was several months before he began gaining strength and weight. (Ryrie cautioned in his report that each batch of the dye should be tested on animals, as the chemical is not constant in its reactions.)

SUMMARY

Early cutaneous as well as neural leprosy often presents difficulty in diagnosis. Instances in which bizarre manifestations of the disease were predominant features are recorded.

The period of incubation is variable. The insidious onset of the disease may account for the so-called long period of incubation.

The histopathologic picture is not always pathognomonic and cannot always be depended on to substantiate the diagnosis. A fibroblastic reaction in tissue seems coincident with a scarcity of organisms.

Methods of finding the bacilli are discussed.

Treatment by other means than chaulmoogra oil is discussed.

714 Medical Arts Building.

ABSTRACT OF DISCUSSION ON PAPERS BY DR. McCOY AND DR. LEHMANN

Dr. Ralph Hopkins, New Orleans: I should like to discuss one phase of these two interesting and important papers: the great incidence of leprosy in families in Louisiana. The chart shown here, which was previously published and to which additions have been made to indicate new cases, shows a rather unusual reversal in the chronologic sequence of the development of cases. The grandparents were among the last of the family to acquire this disease. In one family group both husband and wife, seven of their nine children and one grandchild were lepers. In another family group one mother, one of her sons and eight of her grandchildren were lepers. The eight grandchildren were brothers and sisters. Instances of conjugal infection were astonishingly few.

Dr. O. E. Denney and I made a survey of the histories of thirty-six families from whom histories were obtainable, and in those thirty-six families there were 119 lepers. Of the inmates of the United States Marine Hospital, all of whom came from the state of Louisiana, 33 per cent were as intimately related as parent to child, brother to sister or uncle or aunt to nephew or niece. There were five instances in which there were a father and one or more of his children; there were fourteen

39. Ryrie, G. A.: A Preliminary Report on the Action of Certain Dyes in Leprosy, Tr. Roy. Soc. Trop. Med. & Hyg. **27**:85 (June) 1933.

instances in which there were a mother and one or more of her children. There were fifteen sons of lepers, twenty-one daughters of lepers, thirty-eight brothers of lepers and thirty-one sisters of lepers. Less closely related patients included eight uncles, eight aunts, eighteen nephews, nine nieces, five grandfathers, three grandmothers, five granddaughters and six grandsons.

In Louisiana there are certain parishes in which French is spoken and in which a large percentage of the population is descended from immigrants from Canada, who came to Louisiana at the time described in Longfellow's "Evangeline." In those parishes there is a much larger percentage of leprosy than in the adjacent parishes where English is spoken and where the population is of American ancestry. Leprosy is supposed to have been introduced into Louisiana by these Canadian immigrants, and it is possible that in these people there is a racial strain in which the average level of resistance to leprosy is lower than the average level among the English-speaking population of other parishes in the state.

Louisiana has a large Negro population, and the number of Negroes admitted to the institution is much smaller than it should be in relation to the proportion of Negroes to white men in the population of the state. There are about half as many Negroes as white persons, for their population, among the inmates at the United States Marine Hospital, Carville, La.

It is believed that another source of leprosy in Louisiana was the importation of slaves from Africa. Why the foci then established have not caused a widespread prevalence of the disease in the race in which they have existed for such a long period is difficult or impossible to explain, unless it be accepted that the average Negro has such resistance to leprosy that he remains immune even when exposed to contagion under conditions presumably favorable to the spread of the disease.

Later, when the United States Marine Hospital was established, some interesting statistics were gleaned from the patients admitted from Texas. The number of Texans with Mexican ancestry and with white ancestry among those admitted were exactly equal, although the proportion of persons with Caucasian ancestry to those with Mexican ancestry in the population of Texas is about six to one. In other words, the incidence of leprosy among Mexicans is six times that of Caucasians in Texas.

It can hardly be said that pigmentation of the skin is what makes the Mexican more susceptible and the Negro less susceptible. A more plausible explanation is that differences in degree of resistance in the two races are more than "skin deep" and are inherited racial characteristics.

In the familial relations of Mexicans it is interesting that conjugal infection is rare, while numerous instances of infection in blood relatives occur. A plausible explanation of this fact is that husband and wife may not be equally predisposed by heredity, while in those related by blood the same predisposition may have been inherited.

It would seem that predisposition and exposure to contagion are the factors necessary for the development of the disease.

DR. PAUL A. O'LEARY, Rochester, Minn.: I am pleased that I was asked to participate in the discussion of these excellent presentations by Drs. Lehmann and McCoy, because I was thus stimulated to inquire into the status of leprosy in the state of Minnesota. Dr. A. J. Chesley, of Minneapolis, the executive officer, and Dr. Orianna McDaniel, of Minneapolis, the director, of the Minnesota State Department of Health, supplied data, and Dr. R. R. Sullivan, of Rochester, Minn., compiled them for me.

Some of the members, no doubt, are unacquainted with the fact that forty odd years ago the northwest—Minnesota in particular—was a source of concern to public health officials because of the many lepers living there. The reason for the comparatively large number of lepers in this area is obvious after reading Hansen's report of his visit to Wisconsin, Minnesota and the Dakotas in 1888 to determine the effect of the change of environment on approximately a hundred and sixty lepers who had left Norway some years previously. He was able to examine only thirteen; the remainder, with the exception of three or four, were dead. In Minnesota a diagnosis of leprosy had been made in ninety-eight reported cases since 1890; six of the patients are alive, of whom five are at the United States Marine Hospital, Carville, La., and one is on parole at present. No case of leprosy has been reported in the state since 1933, and only two cases have been reported in the last nine years. The late Dr. H. M. Bracken's prediction that leprosy would disappear in isolated areas such as Minnesota without segregation of the lepers is apparently coming true. Of the ninety-eight patients, eight were native born and ninety were foreign born—sixty-one in Norway, thirteen in Sweden and the rest in one of ten other countries. Of the eight native-born lepers, seven were from families including one or more lepers, while the eighth had a leprous uncle in Norway and lived adjacent to a leprous family in Minnesota. It is worthy of comment that the disease has as yet not appeared in any of the marital partners of these patients, a potent argument against the sexual transmission of the disease, in this country at least.

The period of incubation in the known cases varied from two and a half to ten years, the short period being that of a girl who showed signs of the disease when 2½ years old. She was born of a leprous mother. Of the native Minnesotans in whom leprosy developed, there was leprosy in the immediate families of all but one. There have been, on the other hand, numerous examples in which one or two members of a family were lepers but in which, even though living in squalid and insanitary quarters, other members have not as yet shown manifestations of the disease.

From long observation of a small group of lepers in Minnesota, many of whom were far removed from their native lands, it would appear that the likelihood of transmitting the disease is small, as only eight cases of secondary infection from the original ninety-eight patients were recognized, and seven of these eight were in four families. Perhaps the large farms common in the state and the great distance between farm homes created a type of isolation which was one factor in the low degree of infectivity of the Minnesota leper. On the other hand, hereditary tendency, as in tuberculosis, seems to be an equally prominent feature.

Dr. Howard Morrow, San Francisco: Until 1922 there was a leper colony in San Francisco, and in that colony the number of patients varied from twenty to twenty-eight. There were three or four deaths each year and from two to four new patients each year. In 1922 the patients from San Francisco were moved to Carville, La. Since then four or five patients a year have come to various clinics or hospitals. They are isolated in various county institutions until there are half a dozen or so to fill a car, for it is cheaper to take a carload than to transport them one at a time. A few lepers in California are on probation from Carville, La. Others have such a mild form of the disease that it does not seem necessary to send them there.

I was particularly interested in Dr. Lehmann's photographs and in the two types of leprosy which he described, one the erysipelatoid type and the other the type of erythema multiforme. Cases of those types are rather rare, and without

other evidence of leprosy diagnosis is difficult. Dr. Lehmann referred to the maculo-anesthetic type, which is sometimes hard to diagnose, because the lesions are not macules but infiltrated rings and in these isolated rings it is difficult to isolate the bacilli. Occasionally the patients must be watched for months before a definite diagnosis can be made.

In relation to Dr. McCoy's paper, I have a few notes which I am sure he does not agree with, and I will apologize to him. It is a difficult task to discuss a paper by such an expert bacteriologist as Dr. McCoy. All micro-organisms thus far obtained in cultures from leprous tissue by competent bacteriologists all over the world belong to the group of actinomyces. They are pleomorphic and optionally acid resistant. Dr. Ernest Walker, of the Hooper Research Laboratory, has confirmed the suspicions of earlier investigators. Much of Dr. Walker's work was done in Hawaii a number of years after Dr. McCoy was stationed there. Dr. Walker expressed the belief that a large percentage of leprotic infections are contracted through the feet by walking barefooted on the ground.

Recently in Java much work has been done by infecting rats that had been given a diet low in vitamins A and B and then rubbing mud into the shaved skin. The experimenters had been of the opinion that this leprosy in the soil was rat leprosy. There were no infections in animals given vitamins A and B.

Dr. Howard Fox, New York: I am sorry the distinguished speaker could not tell why leprosy is not contagious in and around New York, where there are always at least twenty-five or thirty cases. The climate of New York is approximately the same as that of France, where a few centuries ago there were 2,000 leprosariums. There is no well substantiated record of a person's contracting the disease in New York or its vicinity.

Another situation which is difficult to explain concerns a patient with neural leprosy in my service at the Bellevue Hospital. Until five years ago this man had spent his entire life in North Carolina, where the disease is not endemic. Since that time he has lived in New York.

In discussing the difficulty of demonstrating leprosy bacilli Dr. Lehmann mentioned the method of producing an artificial bulla and searching for bacilli in its contents. I tried this method with the aforementioned patient and not only failed to find bacilli but produced a large ugly scar on his leg by this procedure.

For a long time, when studying leprosy in the tropics, I was puzzled by cases of the pure neural type in which there were definitely elevated cutaneous lesions, many of which showed a tendency to circinate configuration. I eventually learned that these cases were instances of the condition first described by Jadassohn as tuberculoid leprosy. Examples of this type of the disease have been described by Wade in a series of articles with beautiful clinical and histologic illustrations. The histologic picture shows a tuberculoid structure consisting of epithelioid, lymphoid and giant cells, with no evidence of necrosis. I present three photographs made in cases which I observed while making a survey of leprosy in the Virgin Islands. The photographs show that these tuberculoid lesions occur in the neural and not in the cutaneous type of the disease.

Although patients with the neural type often live much longer than those with the cutaneous type, it is rare to see a leper who has had the disease for several decades. Dr. Hansen showed me a patient in Bergen, Norway, whose disease was of forty years' duration, and in Jamaica I saw a woman who had had the disease for fifty years, according to the hospital records.

Dr. S. E. Sweitzer, Minneapolis: When I first started to practice medicine in Minnesota a number of years ago there were roughly forty cases of leprosy among

the Norwegian population. At that time Dr. H. M. Bracken was director of health, and he did not segregate the patients at all. He told them to go home. They lived all over the state of Minnesota and were not under any particular regulation. They walked around as any one else did, but practically no one got the disease there. I never could figure out why leprosy did not develop in persons coming from a climate similar to that in Minnesota. They might have had better food in Minnesota. The baby Dr. O'Leary mentioned was the last leper I saw. That patient was brought to my office, and I thought the condition was leprosy, although Dr. McCoy did not think so. The patient is still alive. I think leprosy has been pretty well eradicated from Minnesota, but I cannot figure out why there is no spread of leprosy in the northern part of the country, while in the southern part it occurs.

Dr. Hamilton Montgomery, Rochester, Minn.: I wish to emphasize the occurrence of lesions resembling urticaria and erythema multiforme in the early exanthematous stages of leprosy. I reported a case with such manifestations (Proc. Staff Meet., Mayo Clin. **2**:182-183 [Aug. 17] 1937). The patient was born in Wisconsin and had not been out of the country. He was first seen in one of the medical services because of cyanosis of the legs, which was thought possibly due to erythromelalgia, and because of supposed chronic urticaria. He presented large, generalized urticarial wheals, practically all being evanescent. Further examination revealed ulceration of the nasal septum, from which Bacillus leprae was demonstrated. Involvement of the ulnar nerve and a perineural infiltrate appeared in a specimen for biopsy from one of the urticarial lesions. Several years later I saw the patient at Carville, La., at which time he had frank leprosy of the mixed type.

Dr. Fred D. Weidman, Philadelphia: Dr. McCoy indicated that little is known about the diagnosis of leprosy in all its aspects and about its mode of transmission. Additional knowledge of any kind will therefore be welcome, particularly in respect to its etiologic agent. I think that the data Dr. L. G. Beinhauer reported in connection with sarcoid may apply to leprosy. In a recent visit to Pittsburgh I discussed this question with him, and he stated that he too had considered the possibility that nonacid-fast strains, including diphtheroid forms represented stages in the life cycle of the bacillus of leprosy. The similar histologic pictures in some cases of leprosy and of sarcoid, the fact that in many cases the leprosy bacillus cannot be identified, and the fact that the gross morbid anatomic picture is often that of sarcoid are parallel circumstances that create suspicion that the organism of leprosy is similar to that of the noncaseating type of tuberculosis of Beinhauer and Mellon. Too, there might be differences in the constitution of the subject (in the sense in which Draper and Pende used the term) or in the diet which might throw some light on the transmission of this disease.

Dr. Sigmund Pollitzer, New York: In the metropolitan district of New York, with a radius of about 20 miles, there have been a considerable number of lepers, estimated at times at perhaps 100. The New York Health Department requires that all cases be reported but concerns itself only with those in which the patient is living in a crowded tenement under bad hygienic conditions or has open lesions in which bacilli can be demonstrated. The department keeps an eye on its lepers to the extent of having an inspector visit then once or twice a year but otherwise does not bother them. I think this a sane attitude and one which tends to prevent the hysteria in regard to this disease that is so common throughout the country. In all the years of the health department's activity there is no record of leprosy having been acquired in New York.

DR. C. F. LEHMANN, San Antonio, Texas: I shall show slides taken in one case that I did not have time to discuss before in connection with my comment on tuberculid. On the back there are depigmented lesions with raised and infiltrated borders as in tuberculid. The next slide is from the border of one of these lesions, and the following one is from the border of another lesion. I was disappointed in not finding a good sarcoid structure there or bacilli. The condition here is more or less of an end-process, I take it.

It is interesting to speculate on the mutation forms of leprosy. All cultures have yielded diphtheroid or coccoid types. Every laboratory worker who has had any results at all has found a diphtheroid type. It is interesting to speculate on this in connection with the material Dr. Beinhauer presented tonight. From that I have deduced this thought—I may be wrong but it is an interesting conjecture—that the varying histopathologic pictures may be due to mutation forms of the organism in the body. In other words, the histologic picture depends on which form is present in the tissue. Certainly if anything more is ever found out about this disease the information will have to be obtained from studying the organism, early involvements, bizarre manifestations and the hosts. Drs. McCoy and Hopkins both made pertinent remarks in this connection. In my series there were seven white patients. All the rest were Mexicans. Mexicans are susceptible to tuberculosis, and Mexican children are susceptible to glandular tuberculosis. Negroes do not have the glandular type of the disease as commonly as do Mexicans.

I agree with Dr. McCoy concerning isolation. Legally, these patients do not have to be isolated in Texas. My practice is, if they do not practice strict hygiene, to report them and have them sent to Carville, La. If the patient has no open lesions and will practice moderately good hygiene, I take no steps to have him isolated. The legislature appropriated $12,000 in 1909 to arrange for a leprosarium. The amount was raised to $25,000 in 1917, but there was so much controversy in connection with the selection of an appropriate site that the bill was repealed in 1919.

DR. G. W. MCCOY, Washington, D. C.: Dr. Hopkins' experience in finding familial infection is practically the same as mine.

I wish to thank Dr. O'Leary for the figures for Minnesota, which substantially agree with mine. In regard to the case in the third generation, I question the diagnosis of leprosy. There is no fourth generation in Minnesota.

Several have asked the question why leprosy does not spread in New York and why it spreads in various other places. That is a great problem, and the man who solves it will have made for himself a reputation equal to that of Hansen.

PEMPHIGUS: TREATMENT WITH SULFANILAMIDE

PRELIMINARY REPORT

MARCUS RAYNER CARO, M.D.
CHICAGO

In 1935 Domagk [1] demonstrated that an azosulfonamide compound (the hydrochloride of 4′-sulfamido-2, 4-diamino-azobenzene) possessed therapeutic activity against streptococcemia in mice. Later experiments showed that a different compound, para-aminobenzenesulfonamide base (sulfanilamide) was equally effective.

During the past two years there have been numerous reports of striking results obtained from the use of sulfanilamide in human beings. Not only have patients with streptococcic infections, such as streptococcic angina, puerperal sepsis and erysipelas, responded well to treatment, but those suffering from epidemic meningitis, pneumonia and gonorrheal urethritis have experienced similar results.

There is a natural tendency to try a new potent remedy in many diseases, in the hope that it may be of benefit. The use of sulfanilamide in pemphigus was suggested by the article by Welsh [2] in which he reported isolating a specific streptococcus from the blood of patients with pemphigus.

REPORT OF CASES

CASE 1.—S. F., a Jew aged 52, was first seen on May 15, 1937. He had diabetes mellitus, for which he was receiving dietary treatment and injections of insulin. For about three weeks vesicles had been developing on the trunk and the head. At the time of examination there were many flaccid vesicles and bullae on a non-inflamed base and many eroded and crusted lesions. Examination of the blood by the phytopharmacologic test (Pels-Macht) gave a reading of 46 per cent.

Treatment was instituted with sulfanilamide orally, 5 grains (0.3 Gm.) four times a day. The dose has been kept small so as not to interfere unduly with the equilibrium established for diabetes. No local treatment has been used. While the response in this case has not been spectacular, there has been rapid epitheliation of eroded lesions. Although the drug has been used here in doses much smaller than those recommended for other diseases, the patient's condition after treatment for one month is considerably improved.

From the Department of Dermatology and Syphilology, University of Illinois College of Medicine, service of Dr. Francis E. Senear.

1. Domagk, G.: Ein Beitrag zur Chemotherapie der bakteriellen Infektionen, Deutsche med. Wchnschr. **61**:250 (Feb. 15) 1935.

2. Welsh, A. L.: Specificity of a Streptococcus Isolated from Patients with Pemphigus, Arch. Dermat. & Syph. **30**:611 (Nov.) 1934.

CASE 2.—D. P., a Jewess aged 55, was seen on June 18, 1937. She had been suffering from pemphigus vulgaris for about one year and had been under treatment for nine months. During this time the usual forms of therapy had been used. The condition had been growing progressively worse, and at the time of examination the patient was nearly moribund. The entire cutaneous surface was covered by bullae, crusted lesions and large denuded areas. Fissures were present on the groins, and there was considerable edema of the hands and the feet.

All other treatment was discontinued, and sulfanilamide was given by mouth, 10 grains (0.6 Gm.) six times a day, each dose followed by 15 grains (0.9 Gm.) of sodium bicarbonate. Applications were made twice daily of a jelly containing 5 per cent tannic acid. On the second day under observation the patient's temperature rose to 102 F. The dose of the drug was reduced to 10 grains five times a day. On the fourth day the temperature returned to normal, and the patient felt stronger and more alert mentally. No new lesions had appeared, and the large denuded areas were showing epitheliation. The dose of the drug was reduced to 5 grains five times a day. At the end of one week of treatment no new lesions had appeared. Most of the eroded areas had healed completely, and the large crusted lesions were healing rapidly.

The sudden ending of the downward course of the patient and the rapid improvement in her condition within one week were startling.

These patients have been observed for so short a period that conclusions as to the final outcome of the disease are not justified. Both patients may be having a spontaneous remission that is coincidental with the administration of the drug. Only time can tell whether in sulfanilamide there is, at last, an effective remedy for pemphigus. Because the prognosis in pemphigus has been hopeless, these preliminary findings are being reported so that the treatment may be tested more extensively.

25 East Washington Street.

A NEW METHOD OF MAKING MULTIPLE PATCH TESTS

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CINCINNATI

All who must frequently perform multiple patch tests are dismayed by the limitation as to the number of tests it is possible to make at one visit. The forearms are usually the areas of choice, but owing to the limited space it is necessary to use the trunk in addition when one desires to apply many patches. One great disadvantage of patch tests made on the trunk is that during sleep the patient frequently tears off the patches when tossing about.

The object of this article is to suggest the use of a new method of applying patches so that from twenty-five to forty instead of from four to six tests may be made on the forearms at each sitting.

Figure 1 shows a forearm on which patches have been applied according to the method in present use. A small square of blotting-paper containing the substance to be tested is covered with cellophane. The edges of the cellophane in turn are fastened to the skin by means of strips of adhesive tape. It is evident that two tests may be made on each forearm and with crowding, three tests.

When this method of testing is used it is difficult to obtain the cooperation of the patient to return as often as is required for more tests. The result is that the patient is tested with an incomplete series and consequently has less chance of having all of his trouble makers discovered. In an experiment currently performed, the following method of making patch tests presented itself to me.

One strip of wax-paper about ½ to ¾ (1.2 to 1.9 cm.) wide is placed along the length of the forearm. One end of the wax-paper is fastened above the wrist with a strip of adhesive tape from ½ to 1 inch (1.2 to 2.5 cm.) wide (fig. 2). With an indelible skin pencil a numeral is placed on the skin. Immediately adjacent to this numeral is placed a small square of white blotting-paper impregnated with the substance to be tested. A narrow strip of adhesive tape is then placed on the forearm above the tested substance, to limit the motion of the small square of white blotting-paper. The numeral "2" is written immediately above this last piece of adhesive tape, and the second substance to be tested is placed adjacent to this number. This procedure is repeated until from twelve to twenty patches are placed on each forearm. Figure 2 shows the number "10" placed on the skin, which is to be covered with the wax-paper after the tenth substance to be tested

From the Allergy Clinic, Cincinnati General Hospital, University of Cincinnati, College of Medicine.

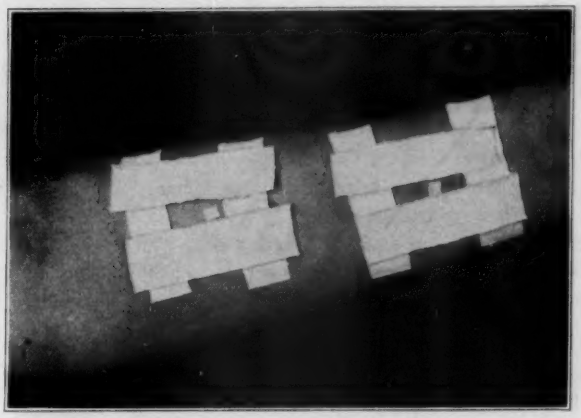

Fig. 1.—Present method of applying patch tests.

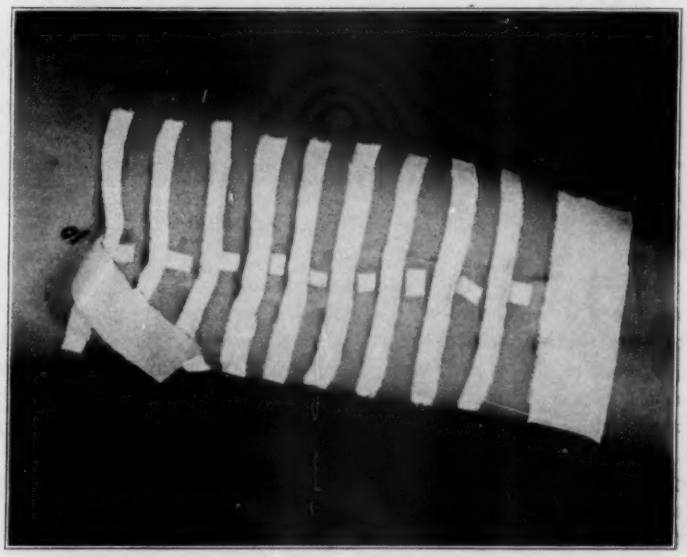

Fig. 2.—Method of fastening the wax-paper above the wrist.

has been placed on a small square of white blotting-paper, which in turn is placed adjacent to the numeral. It is necessary to place the number underneath the waxed paper, for if the numeral is covered by adhesive tape it will not be found when the tape is removed. After the substances to be tested have been placed adjacent to their respective numerals, a notation of their respective position is made so that forty-eight hours later when the adhesive tape and the wax-paper are removed the number adjacent to which a reaction is observed could be properly identified. When all the substances to be tested on the forearm have been applied, the end of the wax-paper nearest the elbow is fastened to the skin by a strip of adhesive plaster similar to that fastening the other end of the wax-paper near the wrist. The wax-paper is fastened bilaterally to the skin by two strips of adhesive tape each from ½ to ¾ inch (1.2 to 2 cm.) wide. This encloses each substance tested in its own small squared area containing its identifying number (fig. 3, upper portion). A third strip of adhesive tape from ½ to ¾ inch wide is then placed

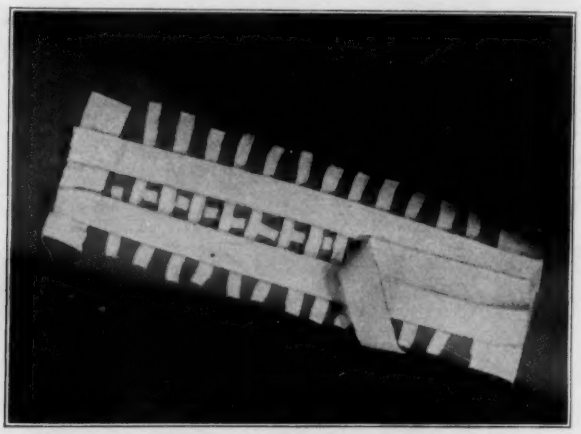

Fig. 3.—Method of applying adhesive tape to protect the wax-paper.

on the uncovered portion of the wax-paper (fig. 3). This is permitted to remain on the skin for forty-eight hours. The adhesive plaster, wax-paper and blotting-paper are then removed. The substance causing the dermatitis is identified by the number adjacent to the area showing a reaction. Should any special test substances cause intense itching before forty-eight hours have elapsed, the square of impregnated blotting-paper causing the itching is removed, its number is recorded. and the rest of the substances to be tested are permitted to remain the entire forty-eight hours before being removed.

More than one row of substances may be tested on each forearm by using wider strips of wax-paper, with strips of adhesive plaster between each row.

SUMMARY

A new method for the application of patch tests is presented in order to enable the physician to perform more patch tests on patients at each visit.

LIPOIDOSIS CUTIS ET MUCOSAE (LIPOID PROTEINOSIS OF URBACH)

REPORT OF THE DISEASE IN TWO SISTERS, WITH A HISTOLOGIC AND HISTOCHEMICAL INVESTIGATION IN ONE CASE

FRED WISE, M.D.

AND

CHARLES R. REIN, M.D.

NEW YORK

Many contributions dealing with disturbances of fat metabolism have been published in recent years and have furnished much new and valuable information to both the internist and the dermatologist. Among these (to mention only a few) are the lipoid studies in xanthoma of Wile and his collaborators,[1] the investigations of Schaaf and Werner [2] in Bloch's clinic on the pathogenesis of xanthoma, several publications by Finney, Montgomery and New [3] and by Weidman and Schaffer,[4] dealing in part with xanthoma of the skin and the larynx, involvement of the latter being of particular interest in connection with other varieties of lipoid involvement of the mucosae. Urbach [5] in a scholarly expo-

Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 4, 1937.

1. (*a*) Wile, U. J.; Eckstein, H. C., and Curtiss, A. C.: Lipid Studies in Xanthoma, Arch. Dermat. & Syph. **19**:35 (Jan.) 1929. (*b*) Eckstein, H. C., and Wile, U. J.: Lipid Studies in Xanthoma, J. Biol. Chem. **87**:311, 1930.

2. (*a*) Schaaf, F., and Werner, A. J.: Pathogenesis of Xanthoma: The Relations of the Cholesterin, Phosphatide and Total Fat Content of the Blood to the Origin of Xanthoma, Arch. f. Dermat. u. Syph. **162**:217, 1930. (*b*) Schaaf, F.: Experimentelle Beiträge zur Pathogenese der Xanthome (Xanthomentstehung und Lipoidstoffwechsel beim Kaninchen nach Lanolinfütterung), ibid. **175**:279, 1937.

3. Finney, W. P.; Montgomery, H., and New, G. B.: Xanthoma Multiplex: Two Cases Involving the Larynx and Trachea, and Associated with Diabetes Insipidus, J. A. M. A. **99**:1071 (Sept. 24) 1932. New, G. B.: Xanthoma of the Pharynx and Larynx, Arch. Otolaryng. **22**:449 (Oct.) 1935.

4. Weidman, Fred D., and Schaffer, H. W.: Xanthoma of the Skin and Larynx Associated with Carcinoma of the Stomach, Arch. Dermat. & Syph. **34**: 767 (May) 1937. Weidman, Fred D.: Position of "Pseudodiabetic Xanthoma" Among the Lipoid Disturbances of the Skin (Urbach), ibid. **34**:814 (May) 1937.

5. Urbach, E.: Lipoidstoffwechselerkrankungen der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pt. 2, pp. 238-374.

sition has added much to the knowledge of several new varieties of lipoid disturbances; these, together with lipoidosis cutis et mucosae, form a group of generalized lipoid diseases with cutaneous manifestations, embracing xanthomatosis, necrobiosis lipoidica diabeticorum and extracellular cholesterosis.[6] In this country dermatologists have become more familiar with the two last-mentioned anomalies of fat metabolism, chiefly through the publications of Michelson and Laymon [7] and Zeisler and Caro.[8] These authors contributed their investigations on necrobiosis lipoidica; recently Laymon [9] presented an excellent study of the first American example of extracellular cholesterosis. Tripp [10] reported the first American case of lipoidosis cutis et mucosae in 1935.

The name lipoidosis cutis et mucosae was given by Urbach to a disease characterized by certain well defined clinical, histologic and histochemical features. These features differ in many respects from those peculiar to other disturbances and anomalies of lipoid metabolism which are regularly accompanied by changes in the skin.

Clinically lipoidosis cutis et mucosae is manifested by infiltrations into the skin and the mucous membranes, consisting mainly of lipoid deposits. A constant clinical symptom is hoarseness, resulting from involvement of the pharyngeal and the laryngeal mucosa.

Histologically the outstanding features in both the skin and the mucosa are, first, an infiltration of lipoid substance surrounding the vascular walls in the form of sheaths and mantles, with massive deposits of lipoid in the cutis and, second, vacuolation of the infiltrating masses in paraffin sections. Foam cells and Touton giant cells do not occur. There is absence of double refraction. These histologic features indicate that the infiltrating substance does not consist of cholesterol esters.

Histochemically the infiltration has been shown to be composed of a lipoid which is soluble in boiling acetone and in hot absolute alcohol. In xanthoma, on the other hand, the lipoids are soluble in hot alcohol but insoluble in boiling acetone. This difference led Urbach to assume that he was dealing with a chemically different substance in lipoidosis cutis. As only a relatively small proportion of the homogeneous infiltrate

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6. The group includes hepatosplenomegaly of Bürger and Grütz, a lipoidosis of the skin and the mucosa.

7. Michelson, H. E., and Laymon, C. W.: Necrobiosis Lipoidica Diabeticorum, J. A. M. A. **103**:163 (July 21) 1934.

8. Zeisler, E. P., and Caro, M. R.: Necrobiosis Lipoidica Diabeticorum, Arch. Dermat. & Syph. **30**:796 (Dec.) 1934.

9. Laymon, C. W.: Extracellular Cholesterosis, Arch. Dermat. & Syph. **35**: 269 (Feb.) 1937.

10. Tripp, Ralph M.: Lipoidosis Cutis et Mucosae, New York State J. Med. **36**:619 (April 15) 1936.

can be dissolved by hot alcohol or boiling acetone, it has been assumed that the lipoid is bound to a protein.

On the basis of his investigations Urbach stated the belief that the disease is a definite clinical entity, bearing the impress of an inborn error of metabolism and characterized by a generalized and localized disturbance of lipoid metabolism. He stated that the process is an infiltrative one (analogous to amyloid infiltration) and not degenerative. In the majority of patients potential diabetes exists. Urbach identified the infiltrative deposits as lipoids belonging in the group of phosphatides soluble in boiling acetone (lecithin). His histochemical studies led him to believe that these lipoids are bound to a protein by a physical-adsorptive process. To emphasize this participation of the albumin component, he suggested the designation "lipoid proteinosis." From the standpoint of its pathogenesis, Urbach identified the disease as a "phosphatide lipoidosis."

The mucosal manifestations were first described by Wiethe [11] in 1924. He expressed the belief that the disease consists of local deposits of hyalin in the upper portion of the respiratory passages. In 1928 Urbach undertook a thorough investigation and together with Wiethe [12] described nine cases occurring in four families. Between 1930 and 1934 Urbach [13] observed several new cases. Two additional cases were reported in the following year by Bénesi [14] and Hoffmann.[15] Kindler [16] reported another example in 1932. Schreus [17] presented a case before the Rhenish-Westphalian Dermatologic Society in 1935, and Haxthausen [18] presented a case before the Danish Dermatologic Society in November, 1936.

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11. Wiethe, C.: Ueber lokale Hyalin Ablagerungen in den oberen Luftwegen, Acta oto-laryng. **10**:237, 1926.

12. Urbach, E., and Wiethe, C.: (*a*) Lipoidosis cutis et mucosae, Virchows Arch. f. path. Anat. **273**:275, 1929; (*b*) Abortive Case of Lipoid Proteinosis, Arch. f. Dermat. u. Syph. **168**:94, 1933.

13. Urbach, E.: (*a*) Cutaneous Lipoidosis, Dermat. Ztschr. **66**:371, 1933; (*b*) Lipoidosis with Cutaneous Manifestations, Klin. Wchnschr. **13**:577, 1934; (*c*) Familial Lipoidosis of the Skin and Mucosae on the Basis of Diabetic Disturbance of Metabolism, Arch. f. Dermat. u. Syph. **157**:450, 1929.

14. Bénesi, O.: Zur Kenntnis der Lipoidosis cutis et mucosae, Ztschr. f. Laryng., Rhin., Otol. **21**:60, 1931.

15. Hoffmann, E.: Lipoidosis cutis et mucosae, Dermat. Ztschr. **62**:296 (Nov.) 1931.

16. Kindler, W.: Beitrag zur Lipoidosis cutis et mucosae, Ztschr. f. Hals-, Nasen- u. Ohrenh. **30**:659, 1937.

17. Schreus, H. T.: Lipoid-Proteinosis, Zentralbl. f. Haut- u. Geschlechtskr. **53**:529 (June 20) 1936.

18. Haxthausen, H.: Lipoidosis cutis et mucosae, Zentralbl. f. Haut- u. Geschlechtskr. **55**:514 (March 20) 1937.

COMPOSITE CLINICAL-MORPHOLOGIC PICTURE

The disease affected the skin and the mucosa in all the reported cases. Two varieties of cutaneous lesions have been described, nodular and hyperkeratotic. At certain stages of the disease the varieties may coexist, but one variety predominates. The earliest symptom is hoarseness, which manifests itself in early infancy as a rule and not later than the second year. The nodular and hyperkeratotic lesions in the skin appear much later. In most patients a pocklike eruption appears during infancy and leaves irregularly outlined soft depressed scars.

The scalp in patients of both sexes shows a sparse growth of hair, resulting from an infiltration of papules. In the nodular form of the disease the characteristic changes, affecting chiefly the face, consist of a variola-like scarring, together with a diffuse sepia-brown pigmentation and a scattering of yellowish papules and irregular ridges. The edges of the eyelids show beadlike whitish papules and almost complete loss of lashes. The vermilion border of the lips appears to be dry and has many vertical grooves, especially at the corners of the mouth.

The extensor surfaces of the elbows are the seat of elevated firm, elastic lesions, which are partly brownish violet and partly yellowish white. These elevations are made up of groups of numerous elementary papules closely crowded together.

The proximal interarticular surfaces of the fingers, dorsally and laterally, show millet-sized elementary lesions forming small plaques. These impart a feeling resembling that of a nutmeg grater, and their surfaces appear like that of a mulberry.

In the hyperkeratotic form the papular lesions undergo early resolution and are difficult to demonstrate, although they are prone to persist more conspicuously on the elbows, the knees and the hands.

The mucosal lesions affect the lips, the tongue, the buccal cavity, the pharynx and the larynx. (In one case the inner surfaces of the labia minora were involved.) The lips—the lower more than the upper—show on their inner surfaces fairly firm yellowish white deposits in the form of plaques. Widespread firm yellowish infiltrated plaques occur on the soft palate, the palatal arch, the pterygomandibular ligaments and the under-surface of the tongue. Among these plaques are scattered scarlike depressions. The tongue seems "wooden," and its motion is limited. Although its dorsal surface is not actually yellow, the tongue imparts the impression that a deep-seated infiltration is present, and that is, in fact, demonstrable histologically. The frenum is broadened and thickened, with a deposit of yellowish masses which limit extension of the tongue to the buccal surface of the lips.

The palatal tonsils are covered by a translucent firm mass. The roof of the larynx on its lingual aspect is thickened to double its normal

size by irregular, elevated deposits. The aryepiglottic folds are symmetrically and extensively broadened. The vocal cords, due to deposits of globular masses, are much thickened. At the posterior wall of the larynx these deposits are fused and have the appearance of spinous excrescences.

In the majority of cases there is an increased content of sugar in the blood during fasting or a pathologic sugar tolerance curve following ingestion of food. In three cases there was definite alimentary glycosuria and in one a diabetic blood sugar curve. Two sisters described by Urbach had latent diabetes. Tripp's patient and the parents showed a diabetic tendency.

Inherited factors seem to play an important pathogenic role in the disease. In several cases there was consanguinity of the parents, and familial occurrence, congenital hoarseness and certain developmental defects, such as absence of two lateral upper incisors, sparse growth of the beard and sexual frigidity, have been noted.

In eight of the fourteen cases compiled by Urbach, laryngotomy was necessary to prevent death by asphyxiation. In several patients the lesions regressed after the first pregnancy.

REPORT OF CASES

During the past year two sisters, aged 18 and 5 years respectively, have been under our observation.

CASE 1.—*History.*—Miss E. W., aged 18, a brunette, a Jewess born in Russia, complained of hoarseness and extensive wrinkling and pitting of the skin, mostly confined to the face and present since the age of 6 months. She had lived in the United States since the age of 2 years. Her parents and one sister, aged 14, are alive and well. The father and this sister are markedly obese. Another sister, aged 4 years, has been hoarse from the earliest observable period and has recently begun to show lesions of the skin and mucosa similar to those of the patient. There is no history in the family of metabolic or allergic diseases, nor is any relative known to have the same condition as the patient and her youngest sister.

The past health of the patient has generally been good. In childhood she had diphtheria and whooping cough, and at the age of 4 years her tonsils were removed. There were occasional frontal headaches "from reading." At the age of 9 years she had a purulent discharge, accompanied with tenderness of the left ear, which lasted two or three weeks. Occasionally she had transient pains in the right knee and leg, which were associated with changes in the weather. The patient was moderate in her habits and, although plump, not a heavy eater. She weighed 140 pounds (63.5 Kg.) and was 64 inches (162.5 cm.) tall. The bowels were active, and she slept well.

She was mentally alert, being in the last term of high school, but physically sluggish, since she took no exercise. There was no menstrual irregularity. She was cheerful, had a number of friends and adapted herself well to her illness.

Present Illness.—The mother stated that the patient was hoarse from the time she began to speak. At the age of 18 months "a yellowish blistering" appeared on the back of the neck and soon sloughed, leaving scars. Similar lesions gradually

appeared later, predominantly on the face but on the rest of the body as well. The process soon involved practically the entire skin of the face. Hoarseness persisted, but fresh cutaneous lesions ceased to appear after the age of 13. No connection was noted between diet and the appearance of the lesions. The mother expressed the belief that the cutaneous lesions were intensified in the summer. Therapy was of no avail during the active stage of the disease, and after the age

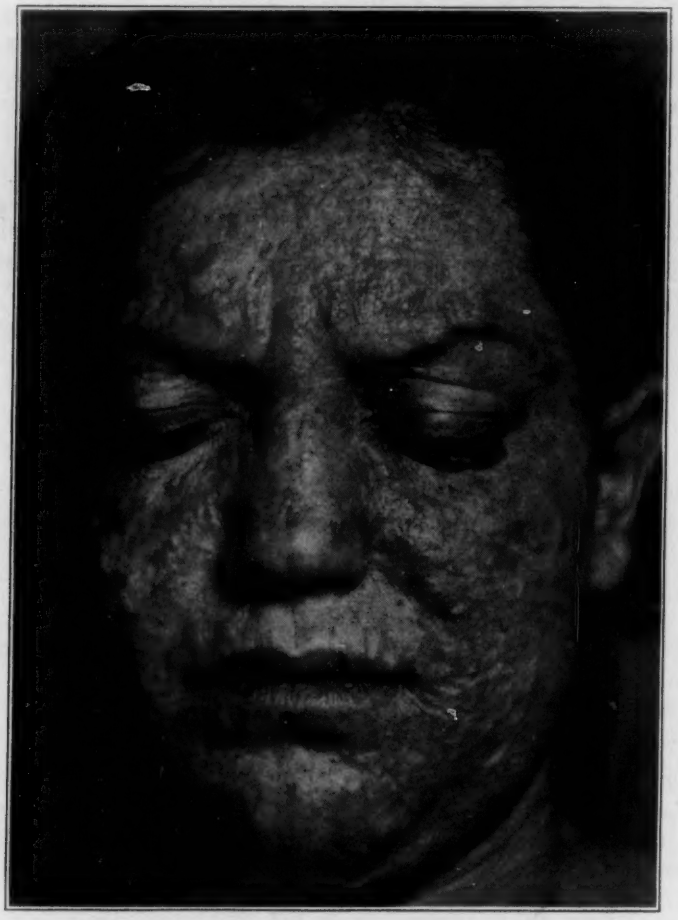

Fig. 1 (case 1).—Lesions on the face of a patient with lipoidosis cutis et mucosae.

of 9 years none was attempted. The patient was admitted to the New York Hospital May 11, 1936, for study. A complete physical examination revealed that the gross pathologic lesions were confined to the labial, buccal and laryngeal mucosae, the scalp and the skin of the face and the neck.

Examination (figs. 1, 2 and 3).—With the exception of the hands and the feet, nearly all regions of the body displayed evidences of a preexisting eruption which had undergone complete resolution, leaving small pocklike pitted scars and larger, slightly depressed scars, the latter resembling those following vaccination. The

Fig. 2 (case 1).—Pitted scars resulting from early lesions.

Fig. 3 (case 1).—Lipoid deposits on the lips and the under-surface of the tongue.

scars were soft, pliable, nonpigmented and usually sharply bordered and varied in size from 0.5 to 2 mm. The small ones were distributed irregularly over the trunk and the extremities, some being widely scattered while others formed isolated groups. The larger scars predominated on the shoulders, the arms, the thighs, the upper part of the back and the back of the neck. (These scars, mentioned by Urbach and by Tripp in connection with their cases, resulted from a pustular eruption which had persisted during infancy and early childhood and which healed spontaneously. The significance of this early eruption is unknown.)

The face and the scalp were the sites of the most prominent cutaneous lesions. The anterior portion of the scalp, from the vertex to the forehead, was brownish yellow, with a roughened, somewhat granular surface, and appeared to be more firm and bound down than the normal scalp. The hair was thin and sparse and appeared lifeless.

The most conspicuous and most strongly developed cutaneous changes affected the face. Here the skin appeared to be thrown into a peculiar irregularly reticulated and honeycombed pattern of shallow scars with elevated borders; this resulted in a combination of depressions from 4 to 10 mm. in diameter and corresponding delicate ridges. When palpated the skin felt firm and elastic. There was absence of definite papule formation, hyperkeratoses or scales. The skin was brownish yellow, but nowhere was there any clinical resemblance to typical xanthoma. The glandular orifices were not enlarged, and there was no evidence of seborrhea or hyperhidrosis. The general surface resembled the cicatrized residual effects of severe hydroa vacciniforme, but the ears were devoid of scars. The margins of the eyelids had an irregular gnawed appearance, showing evidence of a preexisting destructive process, although most of the lashes were preserved. On the point of the left elbow there was a single lentil-sized brownish yellow indurated papule, surrounded by a hyperpigmented zone of soft and wrinkled skin, together with some small pitted scars.

The mucosal lesions were situated on the buccal surface of the lips (most pronounced on the lower), the under-surface of the tongue (with involvement of the frenum) and the palate. The labial lesions consisted of mosaic-like deposits of yellowish papules and small angulated plaques, some discrete and some coalescent. They formed somewhat firm, superficial infiltrations, which seemed to be embedded just beneath the surface of the mucosa. The frenum of the lower lip showed a similar involvement. The under-surface of the tongue, together with the frenum, showed the most profound changes. The frenum formed a hard, solid, inelastic and thickened yellowish white mass; the surrounding tissue was studded with similar indurated infiltrating plaques of the same color and consistency. The dorsal surface of the tongue appeared unchanged but felt more firm than normal. The patient was unable to protrude the tongue beyond the buccal surface of the lips. The buccal mucosa on both sides showed a number of small nodules, from 2 to 3 mm. in diameter, which were barely perceptible but readily palpable. There were ten of these nodules on the left and six on the right side. On the hard palate there were a few small superficial and faintly outlined angulated scars; the soft palate and the palatal arch were the seats of discrete and confluent infiltrated plaques.

The tonsils were prominent and cryptic. The pharynx was slightly injected and granular, owing to the presence of raised yellowish white masses of varying size which gave an impression of a thickened mucous membrane. The epiglottis was involved in a similar process. Direct laryngoscopic examination showed that the vocal cords moved well and freely. The laryngeal mucosa, in common with that of the lips and the mouth, was pale and thickened, especially in the region of the interarytenoid tissues. The thickening of the latter tissues was regarded as the cause of the hoarseness. No nodules were seen on the true vocal cords.

CASE 2 (fig. 4).—H. W., a girl aged 5 years, the sister of E. W., had on both cheeks diffuse and isolated brownish yellow infiltrated plaques, with no evidence of active inflammatory reaction. Scattered over the surface of the face were numerous shallow pitted scars, varying from 2 to 5 mm. in diameter. The lobe of the right ear showed remnants of a group of papules which had undergone partial involution. On the dorsa of the hands and the forearms were numerous small pocklike pitted scars. The lips, the tongue, the buccal mucosa and the tonsils showed a yellowish granular surface, but definite infiltration could not be elicited in any of these regions except the lower lip. The child had been hoarse since the age of 14 weeks. The tongue was bound down to the floor of the mouth

Fig. 4 (case 2).—Lesions on the face of the younger sister of the first patient.

by the infiltrative process in the frenum and surrounding tissue. The tip of the tongue could not be protruded beyond the teeth.

The child appeared to be in normal general health. The parents denied permission to carry out a thorough examination and to obtain a section of the skin.[19]

The elder patient (case 1) was admitted for study to the New York Hospital, under the care of Dr. Arthur W. Grace. Histologic examinations of tissues and chemical analysis of the blood were made during this period of hospitalization by Dr. N. C. Foot of the department of surgery and Dr. Milton J. E. Senn of the department of pediatrics, respectively.

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19. The sisters were presented at a meeting of the New York Dermatological Society, March 24, 1936 (Wise, F.: Lipoidosis Cutis et Mucosae, Arch. Dermat. & Syph. **35**:357 [Feb.] 1937).

LABORATORY INVESTIGATIONS IN CASE 1

1. *Histologic Examination.*—(*a*) Sites of Removal of Biopsy Specimens: [20] Two portions of tissue were removed. The first was taken from an area of the foreheead in which there were many pinhead-sized yellow white nodules. The fresh tissue was somewhat friable and tended to crumble on handling. The second portion of tissue was taken from the clinically normal skin of the back, at the level of the fourth dorsal vertebra.

(*b*) Methods: The portion of tissue removed from the forehead was divided before fixation into four equal parts, each of which was treated separately. The

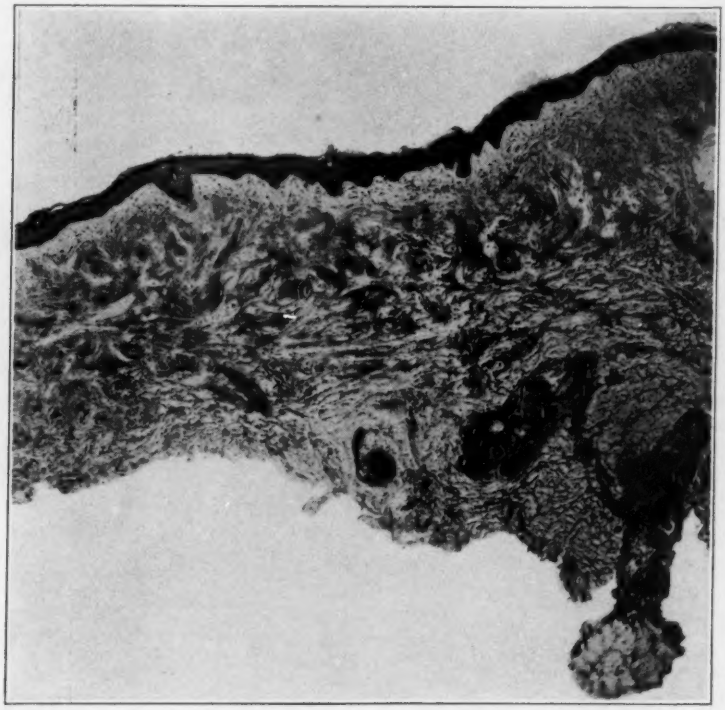

Fig. 5 (case 1).—Frozen section from the face, stained with sudan IV and counterstained with hematoxylin, showing homogeneous structureless material in the corium.

first quarter was fixed in a 4 per cent neutral solution of formaldehyde and cut with the freezing microtome. The sections were stained with sudan IV and nile blue sulfate. The section stained with sudan IV was counterstained with hematoxylin. A second portion was fixed in a mixture containing potassium bichromate, according to Ciaccio's [21] method, and stained with sudan IV and nile blue sulfate. The use of Ciaccio's method allows paraffin sections of materials

20. Permission to excise tissue from the mucosa was not granted.

21. Ciaccio, C.: Pathologic Anatomy and Microbiology of Measles, Virchows Arch. f. path. Anat. **199**:378, 1910.

containing lipoid and fat to be cut without loss of all the lipoid and fat in the dehydrating and clearing processes. A third portion was fixed in a 4 per cent neutral solution of formaldehyde, embedded in paraffin and stained with hematoxylin and eosin. The remaining quarter of fresh tissue was extracted with boiling acetone in a fat-free thimble with Soxhlet's apparatus. An attempt was made to cut paraffin sections of the extracted tissue, to ascertain the extent to which acetone-soluble substances were present in the tissue. The preliminary treatment with acetone, however, rendered the tissue too hard to allow the cutting of sections.

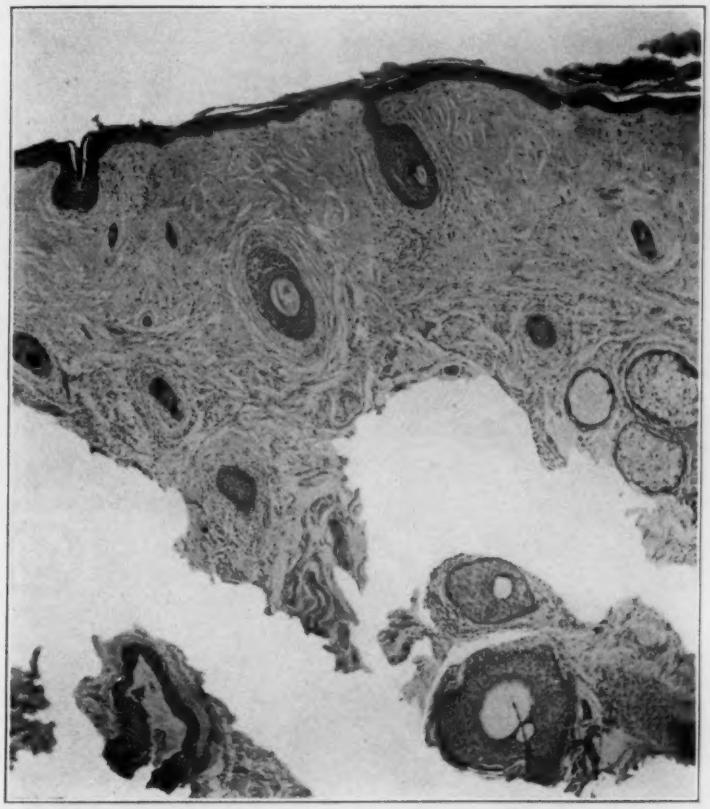

Fig. 6 (case 1).—Paraffin section from the face, stained with hematoxylin and eosin, showing homogeneous material occupying the entire corium. This amorphous material is traversed by numerous clefts, which may have been produced by the solvent action of the agents used in the dehydrating and clearing of the tissue.

The portion of clinically normal tissue removed from the back was divided into two parts. One part was fixed in a 4 per cent neutral solution of formaldehyde and cut with the freezing microtome; sections were stained with sudan IV and nile blue sulfate. The other part was fixed according to Ciaccio's method, embedded in paraffin and stained with sudan IV and nile blue sulfate.

(*c*) Results: Frozen sections from the lesion on the face (fig. 5), stained with sudan IV and counterstained with hematoxylin, showed thinning of the

epidermis, absence of papillae and some hyperkeratosis. The corium presented the most striking appearance, in that it was occupied largely by a homogeneous, structureless material which took a rusty brown stain. This material did not extend right up to the basal layer but was separated therefrom by a band of edematous collagen fibers of approximately the same width as the epidermis. Interspersed in the deposit were numerous irregularly shaped clefts, which may have been produced in the preparation of the frozen section. The sweat and sebaceous glands and the hair follicles were surrounded by the amorphous material, which, how-

Fig. 7 (case 1).—Frozen section of clinically normal skin of shoulder, stained with sudan IV. The corium is filled with small clumps strewn throughout the tissue in the manner of a precipitate.

ever, did not have a special affinity for these appendages. Under high magnification minute globules of an orange-colored substance were observed. All over the corium, especially in the areas where the rusty brown deposit was heaviest, neutral fat appeared in the subcutaneous tissue as large orange-colored droplets, and similar material was present in the keratin layer of the epidermis and in the hair follicles. Blood vessels were sparse throughout the tissue. In the frozen section stained with nile blue, the amorphous deposit in the corium assumed a navy blue tint, and the neutral fat became rose pink. The sections fixed by

Ciaccio's method did not show any lipoid material or neutral fat when stained with sudan IV or nile blue; these sections presented throughout a homogeneous grayish pink under the first stain and a light blue under the second.

Paraffin sections (fig. 6) stained with hematoxylin and eosin showed a material of uniform pink tint occupying the whole of the corium. Adjacent to the basal layer was an ill defined band of approximately the same thickness as the epidermis, in which edematous collagen fibers were present. Differentiation of this band

Fig. 8 (case 1).—Section of clinically normal skin of shoulder, fixed by the Ciaccio method and stained with sudan IV. The small clumps of lipoid material, so evident in the stained frozen sections, could not be detected.

from the subjacent amorphous material was difficult, owing to the fact that both were stained the same tint with the eosin. The amorphous material was traversed by numerous clefts, which may have been produced by the solvent action of the agents used in the dehydrating and clearing of the tissue.

Frozen sections from the clinically normal skin of the shoulder (fig. 7) showed the epidermis to be of normal width, with little hyperkeratosis. The papillae and the appendages were for the most part well developed. The corium was

filled with small clumps which stained rusty red with sudan IV and deep navy blue with nile blue. These clumps appeared to lie strewn throughout the tissue in the manner of a precipitate. That they were not artefacts was indicated by the fact that they were present at all focal levels. There was a diffuse, stippled background of droplets with similar staining properties throughout the entire corium, in the epidermis and in the epithelium of the sebaceous glands and the hair follicles. The keratin layer of the epidermis showed considerable neutral fat, and this substance was found in the sebaceous glands and subcutaneous tissues. It differed from the lipoid deposits in that it stained rose red with nile blue, whereas the lipoid stained navy blue. With sudan IV the neutral fat was somewhat more orange and somewhat less rusty red than the lipoid deposits. Fatty acid crystals were found stained both by sudan IV and by nile blue, but they differed from the deposit in general in that they were acicular and definitely crystalline.

The sections fixed by Ciaccio's method (fig. 8) and stained with sudan IV and nile blue did not show any lipoid material or neutral fat. The sections had a homogeneous tint throughout, grayish pink and light blue under the two stains, respectively, and the small clumps of lipoid, so evident in the stained, frozen sections, could not be detected (i. e., fat was dissolved out in its entirety).

2. *Chemical Analysis of the Blood.*—(*a*) Fatty Constituents of the Blood: Determination of the fatty constituents was made by the method of Kirk, Page and Van Slyke,[22] plasma and red blood corpuscles being used separately. The anticoagulant employed was hirudin. The results are given in the table and show little departure from normal.[23]

Fatty Constituents of the Blood in Case 1

Constituent	Plasma, Mg. per 100 Cc.		Cells, Mg. per 100 Cc.
	Patient	Means of Normal (Adult)	
Total lipoid carbon	470	.....	200
Total cholesterol	172	232 ± 62	121
Free cholesterol	63	82 ± 17	93
Esterified cholesterol	109	.....	28
Lipoid phosphorus	5.8	7.7 ± 3.0	4.4
Phosphides	137	181 ± 71	103
Total lipids	611	735 ± 216	260

(*b*) Dextrose Test: Determinations of sugar in the blood were made according to the method of Benedict before and after the ingestion of 100 Gm. of dextrose. The results which follow differ little from the normal figures:

	Blood sugar mg. per 100 cc.
Fasting	87
Half hour after ingestion	89
One hour after ingestion	144
Two hours after ingestion	70
Three hours after ingestion	57

22. Kirk, E.; Page, I. H., and Van Slyke, D. D.: Gasometric Microdetermination of Lipids in Plasma, Blood Cells and Tissues, J. Biol. Chem. **106**:203, 1934.

23. Page, I. H.; Kirk, E.; Lewis, H. W., Jr.; Thompson, W. R., and Van Slyke, D. D.: Plasma Lipids of Normal Men at Different Ages, J. Biol. Chem. **111**:615, 1935.

3. *Other Examinations.*—Roentgenograms of the chest and the skull revealed no pathologic changes; the frontal sinuses were well developed. The blood count showed 4,200,000 red blood cells, 85 per cent hemoglobin, 12,100 white blood cells, 51 per cent adult polymorphonuclear leukocytes, 3 per cent immature polymorphonuclear leukocytes, 40 per cent lymphocytes, 2 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils. The basal metabolic rate, two days after admission, was —7 per cent. The urine was normal, as was the result of an electrocardiogram. The Wassermann and the Kline reactions were negative.

COMMENT

The histopathologic changes in our sections corresponded in all essential details with those described by Urbach, as observed by him in a patient in the late stage of the nodular variety of the disease.[24]

We were able to obtain only one biopsy specimen from the diseased skin of our patient and one from the clinically normal skin. In the section from the diseased tissue the epidermis was thinned, and the rete pegs were flattened. There was no parakeratosis. The cutis showed a striking paucity of blood vessels, and the dilated and thickened capillaries (present in the early stages) were absent. The histologic changes were dominated by the dense infiltration in the cutis and by the homogeneous mantles which surrounded the sweat and sebaceous glands and the sparse thick-walled blood vessels. The infiltrate appeared in the form of roughly circular homogeneous masses with well defined borders. These were in part separated from each other by well marked, clear clefts, which we assumed to be artefacts produced by the action of dehydrating and clearing agents.

In the clinically normal skin Urbach described the changes found in the early stages of the disease. There were typical lipoid mantles surrounding the blood vessels, though to a much less extent than in the diseased skin. Aside from this, there were few noteworthy changes in the section he described. In contrast with this, the section from the clinically normal skin of the shoulder of our patient showed a corium filled with small clumps of lipoid, which stained deep navy blue with nile blue sulfate and rusty red with sudan IV. Blood vessels being absent, there was no demonstrable evidence of perivascular mantles. Although the entire corium appeared to be permeated with lipoid substance, the epidermis, with the exception of moderate hyperkeratosis, remained unaltered.

24. In one of Urbach's paraffin sections obtained from a patient in an early stage and stained with hematoxylin and eosin, there was a normal epidermis, immediately beneath which the cutis showed definite evidence of edema, due to the presence of many vacuoles. The deeper portion of the cutis was occupied by a dense homogeneous substance resembling connective tissue. There were numerous capillaries filled with dark red homogeneous masses.

In contrast with the results obtained by Urbach with the Ciaccio method of fixation [25] we found that our material, after treatment with bichromate solution, did not show any lipoid substance when subsequently stained with sudan IV and nile blue sulfate. We are at a loss to interpret this finding. Evidence as to the nature of the material which resists the (solvent) action of fat solvents after treatment with potassium bichromate solution is confusing. Thus Kaufmann and Lehmann [26] stated that a distinction between unsaturated neutral fats and the other lipoids is by this method not possible and that only the saturated triglycerides remain unstained.

On the other hand, according to Ciaccio, "lipoid-like substances (protagon) can be demonstrated in sections, because these lipoids are insoluble in agents in which ordinary fats are soluble after treatment with bichromate solutions, while neutral fats, fatty acids and cholesterol do not show this peculiarity" (Unna and Schumacher [27]).

SUMMARY AND CONCLUSIONS

The disease called by Urbach lipoidosis cutis et mucosae is described in two sisters, aged 18 and 5 years. Details of the clinical, histologic and histochemical findings in the elder sister are noted. With the exception of minor features, our observations agree with those of Urbach and Wiethe.

Clinically the disease appears to be a constitutional nevoid and familial disturbance of lipoid metabolism. An estimation of the blood sugar of the mother of our patients showed a diabetic tendency. (The father was not available for investigation.) Our patients had the nodular variety of the disease, characterized by hoarseness, which was most pronounced in infancy, and by infiltrated lesions of the lips, the mouth,

25. The Ciaccio method is a means of fixation intended to eliminate the freezing of sections as a preliminary procedure in the specific staining to demonstrate lipoids. Fixation of small pieces of tissue is done in a solution of 5 per cent aqueous solution of potassium bichromate, 80 parts; solution of formaldehyde U. S. P., 20 parts, and acetic acid, from 10 to 15 drops. The tissue is then placed in 3 per cent aqueous solution of potassium bichromate for from five to eight days, washed in running water for twenty-four hours and passed through increasing concentrations of alcohol. The tissue is embedded in paraffin. Sections freed from paraffin are placed in 50 per cent alcohol and then stained either with sudan IV or nile blue sulfate. (Herxheimer, who prefers scarlet red, stated that the results are the same in general but the tint slightly different.)

26. Kaufmann, C., and Lehmann, E.: Are the Prevailing Methods of Histologic Technic Specific for Differential Fat Staining? Virchows Arch. f. path. Anat. **261**:623, 1926.

27. Unna, P. G., and Schumacher, J.: Lebensvorgänge in der Haut des Menschen und der Tiere, Vienna, Franz Deuticke, 1935.

the tongue and the upper portions of the respiratory passages; there were honeycomb-like lesions on the face, associated with a mottled sepia-brown pigmentation; scattered soft pocklike lesions were distributed irregularly over the trunk and the extremities. The latter gave the impression of previously traumatized or infected skin, which had become more vulnerable to external insults as a result of the underlying general metabolic disturbance. The margins of the eyelids were indented and scarred. The hair of the scalp was sparse and lifeless.

With the exception of a small group of papular lesions on one elbow, there were no such hyperkeratotic or nodular lesions as described by Urbach, with their sites of predilection on the fingers, the knees and the elbows. The upper lateral incisors were retained. There was no gross evidence of endocrine disturbances.

Histologically sections derived from a diseased portion of skin were similar to those of Urbach, in that they showed massive well defined deposits of lipoid in the corium, together with perivascular and periglandular mantles and the characteristic clefts in the cutis.

The clinically normal skin of our patient differed from that of Urbach's, in that, first, frozen sections showed the corium to be filled with small clumps of lipoid, whereas in his case he noted only perivascular mantles of lipoid; second, in our section blood vessels were absent, and, third, we were unable to fix the lipoid by Ciaccio's method.

These observations substantiate those of Urbach and Wiethe in their characterization of a disease entity forming one of the units in a group of lipoid metabolic diseases in which there is coexistence of mucosal and cutaneous lesions.

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ABSTRACT OF DISCUSSION

Dr. Paul E. Bechet, New York: I was much interested in Dr. Wise's report, because my associate, Dr. Tripp, reported a similar case[10] before the Medical Society of the State of New York about a year ago. He and I observed this case for over a year, and the symptoms were much like those in Dr. Wise's case, with a few minor differences. The reticulated appearance of the cheek was much more marked, but the hoarseness was much the same. The history showed the rather frequently observed association of diabetes or potential diabetes with this condition. Both the father and the mother were diabetic. The patient showed a high sugar count in the blood, but the urine was free from sugar. I think Urbach's classification is somewhat arbitrary, for the boy in our case showed, besides the lesions on the face, xanthoma-like lesions on the arm which, had they been examined alone, would have been classified as ordinary xanthoma.

Dr. Erich Hoffmann, Bonn, Germany (by invitation): I present a photomicrograph made in a characteristic case of lipoid proteinosis (lipoidosis cutis et mucosae) observed in my clinic and presented in 1927 at the Dermatological

Congress in Bonn, Germany. In this case deep infiltrations were observed in the skin and the mucosa, together with hoarseness.

Dr. H. J. Templeton, Oakland, Calif.: It was my privilege to see with Urbach one of the patients on whose condition the original report was based. This patient was one of four or five siblings who had the disease. All the others had died of respiratory embarrassment. The patient presented few cutaneous lesions but showed extreme involvement of the tongue and the larynx. So excessive was the involvement of the larynx that when I saw him he was in the department for treatment of conditions of the nose and the throat, where intubation or tracheotomy was contemplated.

Dr. Hamilton Montgomery, Rochester, Minn.: Dr. Wise has given a clear presentation of a case of lipoidosis cutis et mucosae (lipoid proteinosis of Urbach), which presents features distinguishing it from other forms of xanthoma. Further investigation is necessary before dermatologists can be sure that chemically the condition is a disturbance in phosphatide-lecithin metabolism. In the study of future cases I should like to urge observers to make quantitative chemical analyses of the diseased skin for the various lipoids, rather than to depend on different tinctorial staining reactions to distinguish, for instance, between cholesterol, phosphatides and the fatty acids. It has been my experience that stains for various types of lipoids may not clearly differentiate between these lipoids. Mention must be made in connection with disturbances of the phosphatide metabolism of the association of hepatosplenomegaly with lipoidosis of the skin and mucous membrane, described by Bürger and Grütz. I have recently observed a case that belongs in that group.

Dr. Fred Wise, New York: Due credit should be given Urbach and his co-workers for their work on lipoid disease. They have done a tremendous amount of work in this field. As time goes on, the condition will be better studied and understood.

One point of interest is the peculiar pitting of the skin in our two cases. What the lesions scattered over the trunk and the extremities signify is a question. The eruption was not impetiginous, for ordinary impetigo would not result in pitting; nor do the scars resemble ordinary tuberculid. For those of the members who have the opportunity to observe cases of this type it would be interesting to try to trace the nature of the early lesions and their relation to the active condition.

BULLOUS DERMATOSES OF TOXIC ORIGIN

REPORT OF A CASE INVOLVING AN ASSOCIATION WITH CHORIOCARCINOMA

JOSEPH A. ELLIOTT, M.D.
CHARLOTTE, N. C.

Toxic bullous dermatoses have frequently engaged the attention of the dermatologist, as is evidenced by the large number of reports of such conditions in medical publications. In reviewing these reports, however, one is struck with the frequent diagnostic difficulties encountered. A bullous eruption produced by a drug, such as an iodide, a bromide, antipyrine or arsenic, is usually identified by a thorough examination of the patient, along with a carefully taken history. Examination of the blood by suitable methods is valuble in cases in which an eruption is suspected of being due to bromide or iodide. Osborne's [1] microchemical method of examination of tissues for arsenic might be used in such a condition.

Dermatologists agree that in many cases it is impossible to differentiate between pemphigus and dermatitis herpetiformis and that only the ultimate course can place borderline conditions in the proper classification. Grouven [2] expressed the belief that dermatitis herpetiformis is a variant of chronic pemphigus; Nékám [3] stated that the two diseases cannot be separated with certainty either clinically or etiologically, while Krantz [4] said that there are transitional forms and that the dermatologist should keep an open mind regarding these and admit his inability to make a precise diagnosis. Many other American dermatologists have expressed the opinion that these diseases are separate entities, and the fact that they may simulate each other at certain stages does not invalidate the arguments in favor of duality.

Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 5, 1937.

1. Osborne, E. D.: Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, Arch. Dermat. & Syph. **12**:773 (Dec.) 1925.

2. Grouven, C.: Are Pemphigus and Duhring's Disease Sui Generis or Are There Transition Forms Between Them? Dermat. Wchnschr. **99**:1084 (Aug. 18) 1934; abstr., Wise, F., and Sulzberger, M.: Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1934, p. 198.

3. Nékám, L., cited by Grouven.[2]

4. Krantz, W., cited by Grouven.[2]

Baird discussed a case [5] of bullous eruption in a woman aged 50 who had Hodgkin's disease. The lesions were erythematous at first and thought to be insect bites; later they became bullous, and a diagnosis of pemphigus was made. Baird called attention to similar cases and stated that bullous lesions occur with malignant processes. Bogrow [6] reported a case of cancer of the uterus in which there was a foul vaginal discharge and a cutaneous condition presenting the symptoms of dermatitis herpetiformis. After a disinfecting douche the eruption began to improve, and it disappeared promptly after the surgical removal of the necrotic mass. In that case the symptoms were attributed to the absorption of the bacterial toxins rather than to the tumor itself.

The case which I shall report is one of choriocarcinoma with metastasis to the lungs and an extensive generalized bullous eruption. I have been unable to find a report of a similar case.

REPORT OF CASE

An educated American woman aged 43, a blonde, consulted an obstetrician on June 6, 1932, because of slight bleeding from the uterus. At this time she was four months pregnant. She was put to bed and given gonadotropic substance from the urine of pregnant women. The bleeding subsided, and the threat of miscarriage seemed to pass, until two months later, when bleeding recurred at such a rate as to cause her to be sent to the hospital as an emergency patient. Examination revealed a hydatidiform mole protruding from the cervix. Behind this there was a normal 6 month fetus in its own amniotic sac. After delivery the mother made what was considered an uneventful recovery. Six weeks after the delivery an Aschheim-Zondek hormone test for pregnancy (Friedman's modification) was made, and the results were positive. The uterus was of normal size and consistency. A curettement was done, but a microscopic examination of the scrapings showed nothing abnormal. The reaction to the Aschheim-Zondek test continued to be positive, but not so strongly, for the following year. Repeated pelvic examinations showed no change in the uterus. After August 1933 the patient was not seen again by her obstetrician but remained under observation by her family physician. He examined her in May 1934 and found the uterus normal.

She consulted me on July 7, 1934, after a vacation at the beach, because of excoriated papules on her arms and legs, which appeared to be results of insect bites. These disappeared in a few days as a result of applications of a soothing lotion. On July 17 she returned with numerous small vesicular lesions around her ankles. These were situated on erythematous bases. Within a few days similar lesions appeared on her arms and her chest. Many of the vesicles coalesced to form multilocular lesions of the size of a hazelnut. The walls of the vesicles were thick and tough. There was some grouping of the lesions, but this feature was not pronounced. The patient had not taken any drug which might have produced

5. Pemphigus, Cabot Case 22052, New England J. Med. **214**:211 (Jan. 30) 1936.

6. Bogrow, cited by Hartzell, M. B.: Dermatitis Herpetiformis, J. Cutan. Dis. **36**:501 (Nov.) 1918.

the eruption. The chief complaint at this time was severe itching. On July 27, ten days after the vesicular lesions appeared, most of them had disappeared, leaving slight pigmentation. Ten days later there was a fresh outbreak, with more lesions than in the previous attacks. New ones appeared over the whole body, and the itching was intense. All the lesions had erythematous bases, and the blebs gradually got larger. After three weeks of arsenical therapy there were no new ones, and the old ones were undergoing involution. On September 3 there was an acute outbreak of large vesicles, some of which arose from a clear skin. These increased in number, and within a few days they had assumed bullous proportions (fig. 1). Nikolsky's sign was not present. A vaginal examination revealed a firm, smooth uterus the size of a small grapefruit. At this time the temperature was normal, the pulse rate 80 and the respiratory rate 18; examination of the lungs and the heart showed no abnormality. The Wassermann, the Kahn and the Kline reaction of the blood serum were negative. The blood pressure was 170 systolic and 75 diastolic. The Aschheim-Zondek test (Friedman's modification) gave positive results with 10 cc., 1 cc. and 0.1 cc. of urine, while 0.01 cc. produced a negative reaction. The smallest amount producing a positive reaction was one one-hundredth of that usual in the test for pregnancy. The uterus was again curetted and again microscopic examination of the scrapings showed nothing abnormal. A roentgenogram of the chest showed a marked congestion of the upper portion of each lung. Shadows from the bullae made it difficult to interpret the plates. Three days later the examination was repeated, and the roentgenologist reported an increase in the congestion of both lungs, with evident metastasis.

Fig. 1.—Bullous eruption associated with choriocarcinoma. This severe exacerbation occurred about the time metastatic lesions were found in the lungs.

During the first week's hospitalization the patient's pulse rate rose from a low of 70 to a high of 100 and the respiratory rate from 18 to 25. Her temperature was normal at first but soon showed an afternoon rise to 100 F. During this time her chief complaints were intense itching and inability to sleep. The bullae became more widespread, despite arsenical therapy, and soon appeared in her mouth, involving the anterior tonsillar pillars and the posterior pharyngeal wall. On September 15 administration of 4 cc. of viosterol three times daily was begun,

and within a week improvement in the eruption was marked. There were few new lesions, and the older ones were undergoing involution. The oral lesions improved only slightly during this treatment. The administration of viosterol was discontinued to determine the effect, and within a few days there was a definite increase in the number of bullae. Medication with viosterol was resumed, and the cutaneous lesions were soon under control, although the general condition was getting worse and the pulse and the respiration were gradually growing more rapid. Restlessness continued, and large doses of various hypnotics brought only partial relief. On October 3 a roentgenogram showed both lungs to be filled with metastatic lesions (fig. 2). At this time the body was comparatively free from bullae. The urine was normal when first examined; later there were

Fig. 2.—Roentgenogram of the chest taken on Oct. 2, 1934, showing well circumscribed malignant lesions throughout both lungs.

a slight amount of albumin and an increasing amount of pus; no casts or dextrose was present at any time. The red blood cells decreased from 4,650,000 to 3,060,000 and the hemoglobin from 75 to 55 per cent, while the white blood cells increased from 11,800 to 22,500 between September 1 and October 15. The high eosinophil count was 11 per cent and the low 6 per cent. The average differential count was 80 per cent polymorphonuclear neutrophils, 10 per cent lymphocytes, 10 per cent eosinophils and 232,000 platelets. There was 9.4 mg. of calcium per hundred cubic centimeters. The clotting time was normal. Cultures of material from the throat showed a green-producing streptococcus as the predominating organism. A similar organism was isolated from the cervix. Culture of the contents of the bullae gave negative results. Two female rabbits were given

intravenous injections, one of 1 cc. of the patient's serum and one of 1 cc. of fluid from a bulla. Both animals showed mature corpora haemorrhagica in both ovaries at the end of forty-eight hours. The reaction produced by the serum was much the stronger. Three specimens of blood were submitted for the Pels-Macht phytopharmacologic test. Results of this test were reported as 66, 62 and 64 per cent, respectively. These findings may be summed up in one sentence of Dr. Pels' reply: "One can only say that this is a toxic dermatitis of the bullous type, as measured by the test." The patient's condition became more toxic; the cardiac rate increased to above 160, and respirations became fast and shallow. Consciousness was retained until a few hours before her death on October 15, approximately twenty-seven months after her first bleeding, twenty-five months after the hydatidiform mole was extruded and three months after her first cutaneous manifestations.

Necropsy, performed by Dr. L. C. Todd, showed a middle-aged woman of moderately heavy build with striking emaciation. The skin and the mucous membranes were pale. There was no edema. Rigor mortis was pronounced in all extremities, the jaw and the neck. There was no unusual feature about the size or the shape of the head. There was moderate edema of the eyelids; the pupils were moderately dilated and equal. The neck was long and narrow and showed no enlargement of the thyroid or of the cervical glands. The thorax was symmetrical and of average breadth and depth. The abdomen was about level with the costal margin. There was dorsal hypostasis. There were no signs of trauma, surgical wounds or scars. The skin from head to foot was covered with numerous dried gray crusts and showed a few small flaccid vesicles with nonerythematous bases. Between the crusts and the vesicles there were numerous confluent and overlapping rounded areas of skin showing marked depigmentation, in contrast with the color of the normal skin. These, apparently, were areas where previous lesions had completely cleared up and presented on the entire trunk bizarre patterns. The unit lesion seemed to be one with a perfectly rounded outline and a clearcut, sharply demarcated margin. The hair of the head was gray and rather scanty. There was no sign of putrefaction. The orifices of the body showed no abnormality. There was no palpable enlargement of the superficial lymph nodes.

The panniculus was rather scanty over the chest and more abundant over the abdomen and was pale lemon yellow. The muscles were fairly well developed and deep red. The abdominal cavity showed no sign of free gas or fluid and no inflammatory exudation from the peritoneum. The diaphragm was at the normal level. The omentum was rather small and showed a small amount of fat, with no adhesions. The abdominal organs were in normal positions. There were no perforations of the stomach or the intestines. The appendix appeared normal. The mammae were soft and flabby and presented the usual lobulation of the nonlactating stage. The costal cartilages cut with ease. The sternum was flat and showed no softening. Its under-surface was smooth and shining. The bone marrow was red and lymphoid. The mediastinal fat was scanty, and there were no microscopic remains of the thymus.

The pericardium showed no increase in pericardial tension, was of normal thickness and presented a smooth inner surface throughout, but the fluid was moderately increased. The heart was slightly larger than the right fist. There were several small irregular whitish patches in the epicardium, both on the anterior surface of the left ventricle and on the posterior wall near the base. These rubbed off with ease and left a ragged surface. Section of the heart outside the

body showed all valves to be patent, with no endocardial vegetations, no deformity of the valve flaps, the chordae tendineae or the papillary muscles and no mural thrombi. There was a large fibrinous thrombus on the right side, extending from the ventricle through the pulmonary aorta into both main pulmonary arteries. The myocardium was deep brown and rather flabby, and the ventricular walls were thinned. The aorta, just above the valve cusps, showed punctate atheromatous change, but there was no sclerosis about the coronary ostia, and the coronary vessels themselves were not sclerotic.

The left lung showed dense pleural adhesions throughout and was stripped away from the parietal pleura with difficulty, leaving a raw hemorrhagic surface.

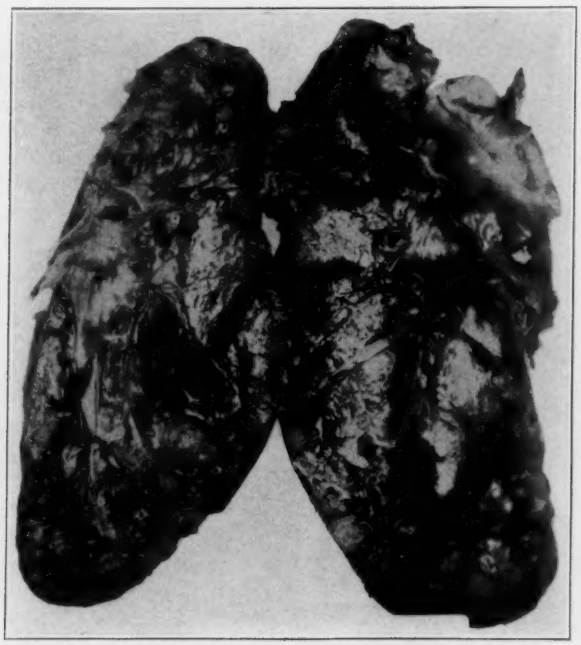

Fig. 3.—Extensive nodules on the surface of the lungs.

The lung itself was reddish blue and showed many large nodules on the visceral pleura (fig. 3). When palpated the lung felt dense and nodular and gave an impression similar to that given by a bag of hickory nuts. Section showed the pleural tissue to be deep red, and many large solid nodules projected above the surface. These nodules were sharply spherical and yellow white in the center. The right lung showed the same type of consolidation and nodular growth as the left. There was more scattering of the nodular growth in the middle lobe, although it contained air for the most part and appeared grayish white.

The peritoneum appeared normal. The spleen was not enlarged and showed no nodular growths. The capsule was somewhat wrinkled, but there were no adhesions. Cut section showed no infarcts or metastatic growths. The pulp was lymphoid. The trabeculae and septums were unusually prominent, but the follicles

were not prominent. The large intestine contained a small amount of semisolid black material. The entire descending colon, the sigmoid flexure and the rectum showed areas of mucosal sloughing. The small intestine showed little abnormality except in the duodenum, where the same mucosal sloughing was noted and numerous punctate hemorrhages were seen. The bile passages were patent. The gallbladder was of normal size, had a normal wall and mucosa and was filled with golden yellow bile. There were no calculi. The stomach showed no perforations, ulcers or new growths but was filled with a small amount of brownish black liquid. At the cardiac end mucosal hemorrhages were noticeable. The liver was large and rather pale brown and showed no nodules. Its cut surface was distinctly tigroid. There was no enlargement of the mesenteric or retroperitoneal nodes.

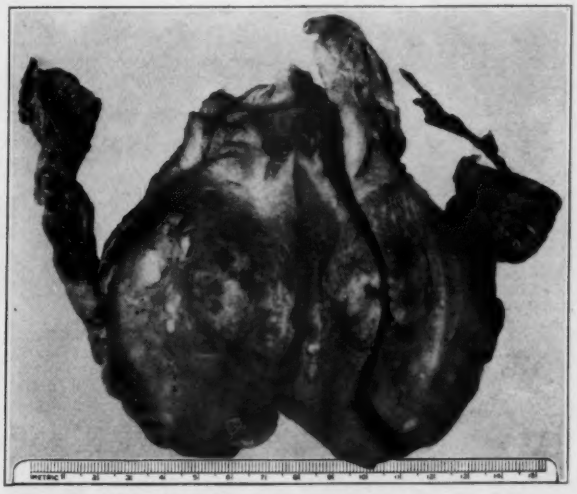

Fig. 4.—Midsection of the uterus showing rounded growths in the walls not connected with the lumen. The sinuses are invaded by the new growth.

The fibrous capsules of the kidneys were smooth and tense; the fatty capsules were not increased in thickness, and the cortical surfaces were bluish red and smooth. Section of the kidneys showed the blood content to be prominent, the cortex light colored and the medullary rays prominent. The pelves, calices and ureters were essentially normal. The bladder was normal. The uterus was markedly enlarged and presented nodular projections both under the perineum covering the posterior surface of the uterus near the internal os and in the region of both horns. The adnexa presented no unusual features. Midsection of the uterus showed two rounded growths in the wall but not connecting with or projecting into the lumen (fig. 4). The cut surface of the growths was yellowish white in the center and hemorrhagic at the periphery. Numerous large uterine sinuses were plugged with this type of growth, which appeared distinctly waxy.

Microscopic examination of the uterus showed the nodule at the right horn to be a fibromyoma. The main masses of growth in the uterine wall and sinuses

were typical chorioma, showing both syncytial and Langhans cells (fig. 5). The liver showed periportal degeneration, fatty infiltration, passive congestion and reticulo-endothelial inhibition of blood pigment. There was medullary autolysis of the adrenals. The kidneys showed passive congestion, acute tubular nephritis and patchy extravasations of blood in medullary rays. The lungs were congested, and there were red hepatization, edema and metastatic growths of chrorionic neoplasm, surrounded by dense masses of canalized fibrin, which showed a brilliant stain with eosin. There were oval, fusiform, round and epithelioid cells, as well as syncytial giant cells with acidophilic cytoplasm. The Langhans nuclei were

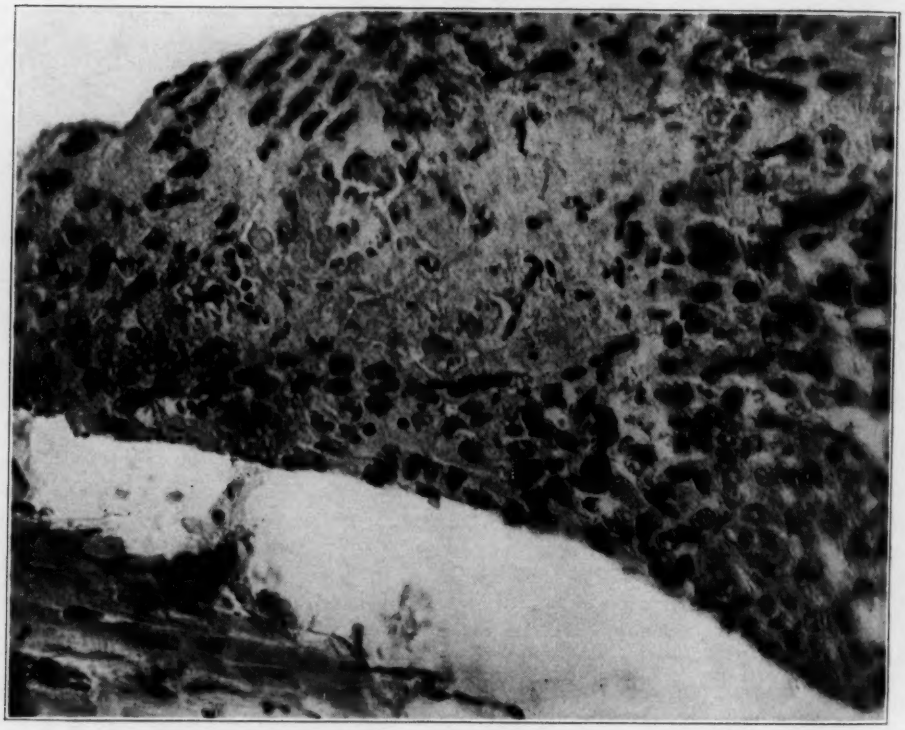

Fig. 5.—Photomicrograph (high power) of the invading neoplasm in the uterus. Proliferating syncytial and Langhans cells are seen in large numbers.

large, stained deeply and showed many atypical mitoses. The central portions of the tumor masses had undergone degenerative changes and necrosis, with loss of structure and staining ability. Actively proliferating Langhans cells at the periphery infiltrated the fibrinous masses and the parenchymatous tissues of the lung proper. In the myocardium the muscle cells appeared atrophic, and there was intercellular edema. There was some diffuse increase in the supporting connective tissue stroma. There was loss in the staining power of the nuclei, and polar pigment was increased. The transverse and longitudinal striations had

disappeared, and there were marked segmentation and fragmentation of the cells of the cardiac muscle.

Section through a vesicle and including the entire cutis (fig. 6) showed a superficial splitting of the rete Malpighii. The vesicle was filled with albuminous fluid and numerous polymorphonuclear leukocytes, but there was no preponderance of eosinophils. The rete was thinner than normal. There was some parakeratosis and a patchy intercellular edema beneath the vesicle, edema of the papillae and a scanty fibroblastic and diffuse lymphocytic and polymorphonuclear infiltrate of the

Fig. 6.—Photomicrograph (low power) of a bulla from the left ankle, showing splitting of the rete Malpighii to form the bulla, which is filled with albuminous fluid and leukocytes. The corium shows a cellular infiltrate.

papillary layer, with some extension along the vessels. There were a few plasma cells. The corium showed a diffuse increase of collagen. The coil glands, hair follicles and sebaceous glands appeared normal.

The pathologic diagnosis was choriocarcinoma, an extensive growth in the body of the uterus, and metastasis to the lungs, with complete consolidation of the entire left lung and of the lower and middle lobe of the right. There was no vaginal metastasis.

COMMENT

The diagnosis of choriocarcinoma was not difficult in my case. The positive reaction to the Aschheim-Zondek test (Friedman's modification) indicated the presence of living chorionic epithelium in the patient, as there were no signs or symptoms of hypophysial disease. This test, according to Potter,[7] depends on the presence in the urine of the gonadotropic principles and perhaps of another, unidentified, hormone. The concentration of these hormones in the urine is a factor of great diagnostic importance. Ordinarily 10 cc. of urine is injected into a rabbit in a test for pregnancy. Smaller amounts often give unreliable results, and some observers use larger amounts. With chorioma, however, the concentration of the hormones is so great that a small fraction of the amount used in the test for pregnancy will produce a positive reaction. The titer in my case was one hundred times that in normal pregnancy, 0.1 cc. of urine producing a positive result. Such a high concentration of the hormone, according to Aschheim,[8] points to chorio-epithelioma.

Ewing[9] divided choriomas into three main types: (1) chorio-adenoma, (2) choriocarcinoma and (3) syncytioma.

In chorio-adenoma the uterus is usually much enlarged, with a thick, honeycombed wall. In cases of advanced involvement the serous surface may present nodular elevations. Chorio-adenoma is of characteristic structure, showing proliferation of all three elements—connective tissue, Langhans cells and syncytium. The connective tissue is compact and cellular but only slightly vascular. The Langhans cells appear in greatly increased numbers and often appear in sheets not connected with the villi. The syncytial buds are large and abundant, with acidophilic cytoplasm. Metastasis is rare and usually limited to the pelvic region but occasionally appears in the lungs.

In choriocarcinoma the uterus is moderately enlarged or of normal size; usually it contains a small compact infiltrating tumor which involves the sinuses. It rapidly traverses or perforates the wall. The structure is highly characteristic, consisting of proliferation of two elements, the syncytium and the Langhans cells. The stroma of the villi is absent. The proportion between the syncytium and the Langhans cells varies, but both are always present. Metastasis takes place early and most frequently to the lungs. Metastases to the vagina are next in frequency; then follow, in order, those to the cerebrum, the liver, the spleen and the kidneys.

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7. Potter, M. F.: The Zondek-Aschheim Pregnancy Test, with Special Reference to Reaction I, J. Obst. & Gynaec. Brit. Emp. **42**:646 (Aug.) 1935.

8. Aschheim, S.: Pregnancy Tests, J. A. M. A. **104**:1324 (April 13) 1935.

9. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1934.

With syncytioma the uterus is much enlarged, has thickened walls and consists of a mass of uterine stroma infiltrated with syncytial cells, fibrin, detritus and hemorrhage. The microscope shows only syncytium, associated with hemorrhage and productive inflammatory cells. Metastasis does not occur.

The clinical course in my case fits that of Ewing's second type, namely, choriocarcinoma. The uterus was moderately enlarged, but no tumor was demonstrable on physical examination. Microscopic examination of material obtained by curetting showed nothing abnormal, owing to the fact that the tumor was situated within the muscular wall. Metastases were discovered a short while after the uterus began to enlarge. The microscopic sections of the tumor and the metastatic growths showed only two proliferating elements—Langhans cells and syncytial cells characteristic of choriocarcinoma.

Since this patient had choriocarcinoma, a product of pregnancy, and since the cutaneous manifestations appeared about the time the chorioma began to grow and increased with the activity of this malignant growth, it seems plausible to assume that the two conditions were closely related. The cutaneous manifestations consisted of recurring vesicles, grouping to some extent, intense pruritus and pigmentation on involution. In the last stages of the disease, bullae appeared from a clear skin, and lesions of the mucous membrane were prominent and persistent. I believe this to be a case of dermatitis herpetiformis, and since it is associated with a product of pregnancy to which I think it is etiologically connected, I classify it as herpes gestationis. The recurring nature of the lesions, the intense pruritus and the pigmentation were factors against a diagnosis of erythema multiforme bullosum.

The diagnosis of pemphigus had to be considered, as the bullae which appeared a month before the patient's death arose from an apparently unaltered surface. There were numerous and prominent lesions in the mouth. Except for these features, there was nothing in the history or findings suggestive of this disease. While involvement of the mucous membranes is rare in herpes gestationis, it does occur. Pringle [10] reported a case in which after the condition had existed for nearly twenty years perforation of the intestine developed and caused death. The eruption got worse after each pregnancy, and the interval between attacks became shorter and shorter, until finally the eruption was present continuously. It involved the mucous membrane of the mouth, the esophagus and the gastro-intestinal tract and finally produced a perforation. Pringle stated that he made the postmortem examination. The phytopharmacologic tests in my case indicated toxemia, but the

10. Pringle, J. J.: Discussion of Little's Dermatitis Herpetiformis, Brit. J. Dermat. **29**:126 (April-June) 1917.

readings were not low enough to be diagnostic of pemphigus. It is true that the readings were slightly lower than the average reported by Pels and Macht [11] for dermatitis herpetiformis, but this can be accounted for by the presence of the extensive chorioma. Carter and Pearce [12] called attention to the frequency of low values for calcium in herpes gestationis. In one of their cases there was 8 mg. per hundred cubic centimeters. My patient was normal in this respect, with 9.4 mg. of calcium per hundred cubic centimeters. A green-producing streptococcus was the predominating organism isolated from the mouth and the cervix. I did not believe that this organism was of etiologic significance, but had Welsh's [13] publication been available at that time I should have submitted a specimen to him for a determination of cataphoretic mobility.

The cause of herpes gestationis is not known. It is thought by many that the cutaneous lesions result from injury to vasomotor nerves by toxins, by ferments from the fetal tissues or by the cells of the chorionic villi. The last-suggested source seems the most plausible, as in many cases the condition appears post partum. Whitehouse [14] reported a case in which the eruption appeared three months after the first delivery and there was a recurrence four days after the second one. MacKee, in discussing this case, stated that in the cases he has encountered the condition appeared after, rather than during, pregnancy. Many other observers have had the same experience. It has been pointed out that in these cases of postpartum involvement the eruption could result from retained placental tags. In this connection it would be of interest to have Aschheim-Zondek tests made to determine whether or not living chorionic epithelial cells are present in sufficient numbers to produce a positive reaction. Results by this test become negative usually about seven days after a normal delivery and from ten to sixteen days after an abortion.

Howard [15] expressed the belief that the substances responsible for herpes gestationis are found in quantity only when the chorionic villi disintegrate and that placental infarctions with dissolution of the tissues are responsible for the periodic exacerbations. Carter and Pearce did

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11. Pels, I. R., and Macht, D. I.: Phytopharmacologic Test in Dermatology: Further Studies and Some Critical Estimations, Arch. Dermat. & Syph. **29**:206 (Feb.) 1934.

12. Carter, B., and Pearce, R. L.: Impetigo Herpetiformis Occurring During Pregnancy, Am. J. Obst. & Gynec. **33**:114 (Jan.) 1937.

13. Welsh, A. L.: Specificity of a Streptococcus Isolated from Patients with Pemphigus, Arch. Dermat. & Syph. **30**:611 (Nov.) 1934.

14. Whitehouse, H. H.: Herpes Gestationis, Arch. Dermat. & Syph. **16**:355 (Sept.) 1927.

15. Howard, R. L.: Herpes Gestationis: Report of a Case, Arch. Dermat. & Syph. **28**:782 (Dec.) 1933.

not support this view, and they reported two cases in which the placenta was normal. In one of their cases the disease ran a course of two hundred and six days after delivery. Werther [16] expressed the belief that the cutaneous manifestations in herpes gestationis are an allergic phenomenon. Sulzberger and Rostenberg [17] pointed out that the presumptive allergen is unknown, and cutaneous testing is therefore impossible.

The treatment of the eruption in my case had, and could have, little influence on the ultimate outcome. As soon as it was evident that the patient had a malignant growth and that the eruption was getting worse with the usual arsenical therapy, it was decided to stop administration of arsenic and to give large doses of viosterol, as advised by Ludy [18] in the treatment of pemphigus. The bullae responded to this therapy, and I was able to keep them under control until the choriocarcinoma caused the death of the patient.

SUMMARY

A case of choriocarcinoma with an extensive bullous eruption is reported.

The course of the cutaneous manifestation fits in with that of dermatitis herpetiformis.

Because the eruption paralleled that of choriocarcinoma resulting from pregnancy, it is suggested that the cutaneous disease be classified as herpes gestationis.

Large doses of viosterol deserve further cautious trial as a therapeutic agent in this disease.

It is suggested that the Aschheim-Zondek test be used in postpartum herpes gestationis to determine if living chorionic villi are present.

ABSTRACT OF DISCUSSION

Dr. Nelson Paul Anderson, Los Angeles: For some time I have been interested in the various cutaneous manifestations which occur during pregnancy, and there are a number of such toxic dermatoses, varying from purely vesicular eruptions to this type of bullous dermatosis, which I believe belong in the group Dr. Elliott suggested, of a special type of dermatitis herpetiformis occurring in connection with pregnancy. With the permission of the chairman I should like to show the picture of a similar condition involving a woman aged 43 whose husband had been dead for about ten years. Because of her widowhood pregnancy was not suspected. The lesions were pemphigoid. Specimens of the blood were sent to Dr. A. L. Welsh at the Mayo clinic, and he reported that the condition

16. Werther, cited by Carter and Pearce.[12]

17. Sulzberger, M. B., and Rostenberg, A., Jr.: Practical Procedures in the Investigation of Certain Allergic Dermatoses, J. Allergy **6**:448 (July) 1935.

18. Ludy, J. B., and Devalin, C. M.: Viosterol in Pemphigus, Urol. & Cutan. Rev. **36**:817 (Dec.) 1932.

probably belonged in the group of dermatitis herpetiformis. So far as I know, this woman is well. She was eight and a half months pregnant, or practically at full term, when this picture was taken (slide). She stated that she had had a similar eruption during her first pregnancy some sixteen years previously, which cleared after delivery.

Dr. Fred D. Weidman, Philadelphia: This tumor behaved true to form in respect to its riotous metastases; only two other tumors compare in this respect, namely, the hypernephroma and the malignant melanoma. I wonder what the determining factor for the complication resembling dermatitis herpetiformis was, i. e., whether it was the necrosis (toxins or ptomains) so notorious in malignant tumors or the gonadotropic substance. From what Dr. Anderson just reported, it appears that the latter may be responsible. Perhaps the reason cases in which there is severe pruritus are not observed more frequently is that the gonadotropic principle is not present in such great quantities in the average pregnant patient. It is not eliminated in the sweat, at least (Gilman, R. L., and Weidman, F. D.: Perspiration: II. Absence of Aschheim-Zondek Hormone in Pregnancy, Arch. Dermat. & Syph. **25**:852 [May] 1932).

I wish to mention a case in which Duhring's disease was shown at necropsy to be associated with bronchiectasis. It had been observed by various Philadelphia dermatologists, including Dr. Schamberg, who made a diagnosis of dermatitis herpetiformis.

Dr. John H. Stokes, Philadelphia: This careful study is helpful to one who, like myself, is caring for a pregnant woman who has herpes gestationis. Chorionepithelioma as a possible complication is new to me. The patient in question has a profoundly allergic background, a dermatitis of the feet suggesting a moderate grade of dermatophytosis with a dermatophytid of the hands and a red and indurated tip of her nose which suggests rosaceaform tuberculosis. The dermatitis herpetiformis resembles erythema multiforme, and in view of the fact that her husband has until recently had open tuberculosis, she may have the erythema multiforme associated with systemic tuberculosis in young women, aggravated by the pregnancy. Her response to arsenic is almost quantitative. Where the dermatophytosis and dermatophytid approach the dermatitis herpetiformis on the forearms and about the ankles, the bullous lesions become impetiginous. Elsewhere they are absolutely sterile.

Dr. H. N. Cole, Cleveland: I think in the case reported it was justifiable to use viosterol in 4 cc. doses, but I think there should be a warning about its use in general in such doses. In a case in which the patient was dying it was justifiable, but the preparation should be used with great care. The members know from reports in the literature what has happened to patients to whom such large doses have been given.

Dr. Bedford Shelmire, Dallas, Texas: Since the members are reporting cases, I desire to add the following:

A gravid woman entered my service at the St. Paul Hospital about Feb. 22, 1927 or 1928. She presented a generalized, severe bullous and gyrate erythematous eruption. Some weeks later she was shown at a meeting of the Texas Dermatological Association, and the diagnosis of a bullous toxic eruption of pregnancy was accepted.

The eruption became so severe that a therapeutic abortion was at one time considered. The eruption continued without remission until she gave birth on June 9 to a baby, normal in every way except for four bullae the size of marbles

or larger on the face, the neck and the chest. These disappeared without treatment in about five days. The eruption of the mother began to disappear rapidly after delivery, and the skin was entirely healed in about two weeks.

The occurrence of bullous eruptions on both the mother and the child was highly suggestive of the toxic nature of the eruption. This was the patient's only pregnancy, and she turned deaf ears to our pleadings to become gravid again.

DR. H. H. HAZEN, Washington, D. C.: Would it not be interesting to take blood from a pregnant woman and give some blood serum to Dr. Shelmire's patient? That might be a safer performance for him than to advise her to become pregnant.

DR. JOSEPH A. ELLIOTT, Charlotte, N. C.: I am much interested in having Aschheim-Zondek tests performed in cases of postpartum herpes gestationis, to determine if living chorionic villi are present. In cases in which the condition is associated with pregnancy it would be interesting to determine the strength of the test, as a high titer might be significant.

Dr. Cole called attention to the danger of giving large doses of viosterol, and his point is well taken. The pathologic changes occurring in the internal organs in my case were studied and are incorporated in the original paper.

COLD THERAPY IN DERMATOLOGY

A NEW FREEZING GAS

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SAN FRANCISCO

The application of cold produces effects varying naturally with the skin's resistance, the temperature of the agent used at the time of contact, the amount of pressure applied and its duration. These effects are useful in a variety of dermatologic conditions.

The local action of solid carbon dioxide has been well known for many years. Since 1906, when I was working in Dr. George Henry Fox's clinic (the Vanderbilt clinic) under Jackson and saw various uses to which solid carbon dioxide was put, I have been using this agent. At that time, to increase the cold, ether was added. Liquid air, being twice as cold, proved somewhat more useful than solid carbon dioxide, but it has always been difficult to obtain and to keep.

For the past few months I have been using a new agent in this field, a freezing gas consisting of butane, isobutane and propane. When sprayed on the skin it quickly produces in the area a temperature of about —40 C.

Several combinations of these substances were first tried on canine and then on human skins. Finally a mixture containing 2.5 per cent butane, 7.5 per cent isobutane and 90 per cent propane was found to be satisfactory.

These gases have the following properties:

Propane (C_3H_8), which constitutes the largest part of the mixture, is colorless, slightly soluble in water and readily soluble in alcohol or ether. It has a density of 1.558 (compared with that of air, which is 1) and a specific gravity of 0.585 at —44.5 C. It melts at —189.9 C. and boils at —44.5 C. Its molecular weight is 44.06.

Isobutane has a molecular weight of 58.08 and a specific gravity of 0.603 at 0 C. Its boiling point is —102 C. and its liquefying point —145 C. It is slightly soluble in alcohol and ether and insoluble in water.

Butane (C_4H_{10}) is a colorless gas, insoluble in water and only slightly soluble in alcohol and ether. It is a constituent of "natural gas."

Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 4, 1937.

Its molecular weight is 58.08, and its specific gravity at 0 C. is 0.601. It boils at 0.6 C. and melts at —135 C. It is insoluble in water and slightly soluble in alcohol and ether.

These gases are toxic but only when a great deal is inhaled, and with the precautions that have been taken no trouble has resulted.

When the gas is sprayed through a small nozzle onto the skin, it will freeze the surface quickly. When gauze or lint is wet with it and applied to the surface with pressure, a similar effect is obtained. The dry gas will not freeze unless an oil is added. Various kinds of insects, including wood ticks, were killed quickly with the spray. Various warty growths and keratoses on dogs were readily destroyed or frozen solid so they could be curetted painlessly. Old infiltrated eczema was relieved more readily and in less time than with coal tar. The gas had a marked antipruritic action. It has been found that various sluggish conditions are influenced favorably through stimulation of the normal functions of the skin by this means rather than through their inhibition by roentgen therapy.

The clinical effects of freezing the skin by these various agents are obvious and may be summarized as follows: 1. Superficial necrosis is produced, its degree depending on the pressure of the agent, the force of the spray, the duration of the exposure and the resistance of the skin. Superficial or deep exfoliation follows in direct proportion to the degree of freezing, the clinical effect being similar to that produced by resorcinol. 2. Stimulation of the circulation and consequent dissipation of infiltration are observed. In this action freezing agents in my experience are superior to coal tar, and results are more quickly obtained. 3. Improvement in the tone of the cutaneous vessels and all the elements in the skin is an important clinical result observed. This effect is particularly useful in acne vulgaris and in rosacea. 4. Local anesthesia is produced rapidly—more so than by ethyl chloride. In fact, the freezing gases will do everything that ethyl chloride will, with the advantage that they do not produce general anesthesia. These preparations are inexpensive. 5. The antipruritic action of cold is well known. The various freezing agents are useful in this respect. Application for varying periods of solid carbon dioxide, liquid air or the freezing gas is helpful.

It must be remembered that these gases are highly inflammable and therefore have to be handled with care. They are heavier than air, and if enough accumulates on the floor, an explosion may result. These gases may gradually settle in the basement of a building and will then constitute a fire hazard. I have been blowing them out of the window with an electric fan and am now working on a vacuum cleaner attachment for pumping them out. Naturally the gas and ethyl chloride are not suitable when the cautery or the electrocoagulation needle is used.

Ethyl chloride produces a cutaneous temperature of only —20 C. (—4 F.), about half that of the freezing gas.

So far, no untoward effects have been noted except dermatitis followed by deep exfoliation where the force of the freezing spray has been too concentrated or applied for too long on one area. In some cases temporary pigmentation has occurred. This action, however, has been of no use so far in vitiligo.

From the foregoing discussion it may be concluded that, in addition to those uses that have been established through this experience, these agents offer other possible uses.

Acne vulgaris of various types, particularly where the skin is sluggish, responds remarkably well. I have noticed this particularly with cystic acne. In cases of acne in which milia or comedones have been localized largely in the areas below the ears and in the temporal region, this procedure has produced satisfactory results. When exfoliation stops, the new skin is found to be softer, thinner, more pliable and free from comedones or milia. This occurs in the treatment of small lesions of adenoma sebaceum. Naturally, the usual attention is paid to underlying bodily conditions, and drainage of the sebaceous glands is promoted by various cleansing lotions and hot and cold applications. I use the spray directly or solid carbon dioxide.

When I utilize solid carbon dioxide I place it in a small gauze bag; the propane-butane gas is sprayed on it; the entire affected areas are stroked with this substance, and light, moderate or heavy pressure is used according to the indications. For the "cold cautery" effect the substance is applied with pressure to one spot for several seconds. Afterward the areas are cleansed with 15 per cent carbon tetrachloride in perfumed spirit. Patients are treated two or three times weekly. In the beginning a patient is seen every other day for a week or so, and all pustules are opened and drained. After that the average patient becomes more cooperative and takes better care of his skin. In most cases great improvement is obtained in less than two weeks. Vaccine therapy and other methods are used when indicated. Success in the treatment of acne depends on full cooperation of the patient. The local superficial freezing therapy seems to be the most useful of all.

Rosacea is helped greatly by judicious cold treatments, as a result of the improved vascular tone that is produced. Possibly the freezing makes Demodex folliculorum more susceptible to other local applications. Naturally, hydrochloric acid, other internal medication and dietetic measures are used when called for.

Lichen simplex chronicus responds surprisingly well, after exfoliation is produced a few times (sometimes only twice). The occipital form is particularly responsive. The gas can be sprayed effectively through the hair. Usually pruritus is relieved early.

Eczema in all forms is helped, the degree of freezing varying according to whether the areas are acute or sluggish. This treatment may supplement or take the place of applications of coal tar.

Dermatophytosis, vesicular, pustular, exfoliating or hyperkeratotic, is made more amenable to other treatment when cold therapy is applied. Normal keratinization of the skin is greatly aided, so this treatment is particularly indicated in the later stages of the disease.

In patches of alopecia areata the freezing spray produces a satisfactory persistent erythema, which is much to be desired.

Nevi, vascular and otherwise, can be destroyed by deep freezing. The spray can be concentrated through a Luer needle attached to the nozzle or through a funnel accurately applied, with pressure around the lesion. Different-sized funnels are kept on hand for this purpose.

Keratoses of various kinds and verrucae can be deeply frozen by the same means and curetted, and the base can be frozen again, with good results.

From the foregoing report it may be seen that freezing therapy is of some practical value in local dermatologic therapeutics.

ABSTRACT OF DISCUSSION

Dr. Marion B. Sulzberger, New York: I think the members all agree with Dr. Alderson that the use of cold therapy is not without its merits in many different types of cutaneous disease and that this modality has proved its value since William Allen Pusey introduced it in dermatology. It seems to me highly questionable whether the dangers of the dermatologist's already sufficiently hazardous existence should be increased by the use of inflammable and explosive gases, when there are available other methods that are just as efficacious. There is a method of applying cold to the skin with solid carbon dioxide dissolved in acetone, a method I learned to employ while working in European clinics. One takes the carbon dioxide, crushes it and mixes it with acetone, making a soft slush of about the consistency of melting sherbet or water ice. This can be spread or painted evenly over large areas with an ordinary cotton swab or applicator. The effect is a superficial escharotic or desquamative one, depending on how often the application is repeated and on how much pressure is applied. With practice this effect can be accurately controlled, and this form of treatment proves valuable for telangiectatic processes, rosacea and some forms of lupus erythematosus.

Dr. Harry E. Alderson, San Francisco: I am trying to reduce the risk of fire as much as possible, and perhaps some combination of solid carbon dioxide, carbon tetrachloride and these gases will be the solution. Every precaution is taken in blowing the gas out of the room. It is not necessary to use much of it, for a slight spray will produce a marked effect in a few seconds. As I mentioned in the paper, I have used acetone and solid carbon dioxide a great deal. Properly handled, these gases are not dangerous.

ZOSTERIFORM LEUKAEMIA CUTIS

ROBERT E. BARNEY, M.D.
CLEVELAND

Leukemic infiltrates in the skin in areas of healed zoster are rare. Only four cases in which the diagnosis has been proved histologically were found in the literature.

Halle [1] reported his observations on two patients with lymphatic leukemia who had been presented before the Silesian Dermatological Society by Jadassohn.[2] One of these patients, a 68 year old man, presented gangrenous herpes zoster in the region of the first and second branches of the trigeminal nerve, with a generalized varicelliform exanthem. The zoster healed with scar formation in about six weeks. Several weeks later an eruption of slightly elevated round infiltrates together with pea-sized papules appeared, not only in the zoster scars but in the areas which had been affected by the varicelliform exanthem. At this time biopsy specimens from both sites showed leukemic infiltrates in the skin.

The second patient, a 71 year old farmer, had zoster over the right side of the body, extending from the lower part of the trunk to the upper part of the thigh. The eruption was more marked over the sacral and gluteal regions. After the zoster healed, a brownish red firm papular eruption appeared on the same site. Microscopically these lesions showed leukemic infiltrates. Halle emphasized the fact that various types of trauma may lead to the development of leukemic infiltrates in the skin, and it may be assumed that herpes zoster, because of its inflammatory character, acts in a similar manner.

Katz [3] reported a case of generalized zoster, the primary eruption occurring on the right side of the face, neck and chest. After healing, leukemic infiltrates were found in the zoster scars. The only other case of this kind was one of subleukemic lymphadenosis recorded by Gottron

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From the Department of Dermatology and the Department of Pathology, St. Luke's Hospital.

Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 5, 1937.

1. Halle, H.: Zoster und Leukämie, nebst Bemerkungen über die Provokation leukämischer Infiltrate in der Haut, Arch. f. Dermat. u. Syph. **159**:238, 1930.

2. Jadassohn, J.: Herpes zoster und varicellenartiges Exanthem und lymphatische Leukämie, Zentralbl. f. Haut- u. Geschlechtskr. **20**:23, 1926; Leukämische Infiltrate in Zosternarben, ibid. **20**:741, 1927; Haut-Leukämie in Zoster-Resten, ibid. **22**:17, 1927.

3. Katz, F.: Zoster bei Leukämie, Arch. f. Dermat. u. Syph. **164**:561, 1932.

and Jacobi,[4] in which the findings were essentially the same as those observed in the first case recorded by Halle.

The rarity of this type of case justifies the following report:

REPORT OF CASE

Mr. C. A., aged 64, was admitted to St. Luke's Hospital on Feb. 11, 1931, complaining of progressive weakness which had been present for eighteen months. Two years before admission he had noticed a small swelling under the right side of the mandible. The swelling gradually enlarged, and similar tumors were noticed successively under the left side of the jaw and in the axillae. For two years he had had difficulty in walking. One brother and a sister had died of tuberculosis. There was no history of cancer in the family. Foot drop developed in his mother and one of his uncles at about the age of 60. His wife and four children were living and well. In 1902 he had had typhoid fever and malaria. There was no history of syphilis.

The patient was a well developed, fairly well nourished man who lay comfortably in bed. The hair of the scalp was sparse, dry and lusterless. The left pupil was slightly larger than the right, but both reacted promptly to light and in accommodation. The teeth were in poor condition, showing numerous carious snags. Examination of the lungs gave negative results. The heart was not enlarged, but a soft systolic blow was heard at the apex. The blood pressure was 158 systolic and 80 diastolic. The spleen was moderately enlarged, and the liver was palpable 2 fingerbreadths below the costal margin on the right nipple line. In the inguinal regions there were a few discrete firm painless lymph nodes the size of a large pea, while in the neck and axillae the nodes varied in size from that of an olive to that of a lemon. In the neck over the thyroid isthmus was a walnut-sized nodule. The genitalia were normal. There were wasting of the muscles of the thighs, arms and hands and a complete bilateral foot drop. The peroneal muscles were full and firm to palpation. A blood count showed 4,050,000 red cells, 90 per cent hemoglobin and 290,000 white cells, 90 per cent of which were lymphocytes. The Wassermann and Kline tests were negative. A small lymph node was removed from the right inguinal region. Microscopically the structure of the lymph node was found obliterated by a diffuse infiltration of round cells somewhat larger than lymphocytes. The nuclei of the infiltrating cells were not quite so dense as those of the lymphocytes, and a moderate number showed mitotic figures. The microscopic picture was consistent with the diagnosis of lymphatic leukemia.

The patient remained in the hospital for ten days, during which time he received roentgen therapy. He was discharged greatly improved, clinically and hematologically. The diagnosis was lymphatic leukemia and familial muscular dystrophy. He was seen again on Nov. 5, 1931, when he was admitted to the hospital for control of nasal hemorrhages. Since his discharge he had continued to receive roentgen therapy. He was referred to the department of dermatology for examination of an eruption involving the right side of the chest. He stated that this eruption began six months before and in the beginning had been suggestive of herpes zoster. The original eruption had never entirely disappeared, the present lesions persisting in the same region without associated symptoms.

4. Gottron and Jacobi: Subleukämische Lymphadenosis cutis nach Herpes zoster generalisatus, Zentralbl. f. Haut- u. Geschlechtskr. **32**:548, 1930.

On general examination the findings were essentially the same as on the patient's previous admission except that the skin was paler. On the vermilion border of the lower lip there were three erosions the size of a small pea. Involving the right side of the chest, following the course of the ninth and tenth intercostal nerves from the spine posteriorly to the midline anteriorly, there was an eruption made up of about six quarter-sized to half-palm-sized groups of papules varying in size from that of a pinhead to that of a large pea (fig. 1). They were yellowish to dull red, infiltrated, painless and noninflammatory. Some of the larger papules had an oval contour, while two on the back were eroded. Two papules were removed from the right side of the chest for histologic examination. At this time the blood count showed 8,400 white cells. The patient remained in the hospital three days. He was readmitted on Dec. 21, 1931, complaining of pain in the right side of the chest and a cough. A diagnosis of bronchopneumonia was made. The patient

Fig. 1.—The zosteriform arrangement of the papules.

failed rapidly and died a week later. Permission for autopsy could not be obtained.

Histologic Examination.—The two papules removed for microscopic examination were fixed in Helly's solution (formaldehyde-Zenker), embedded in paraffin and stained with hematoxylin and eosin. The microscopic studies of the biopsy specimens were made by Dr. R. Dominguez, of the department of pathology.

Microscopic examination showed the lesion to be confined to the corium. The papillae were flattened, and consequently the interpapillary pegs were short and few. The epidermis was otherwise normal. The corium was diffusely and irregularly infiltrated by numerous mononucleated cells. The infiltrate was more dense in some places than in others, giving a focal distribution at low magnification (fig. 2). Although these foci were scattered unevenly in the section, the largest lay deep in the corium, only a few foci being present in the papillary layer (fig. 3). The blood vessels, sweat and sebaceous glands, hair follicles, nerves, and muscles of the corium were involved by the infiltrate, but none of them was systematically affected. The nuclei and cytoplasm of the cells of the infiltrate

resembled lymphocytes in size and general appearance. Another type of cell was found in the larger foci, especially in the centers. These cells were larger, the nuclei were ovoid and less dense, and the cytoplasm was abundant and poorly stained. When this second type of cell occupied the center of a cellular focus, the high power appearance was not unlike that of a lymph follicle (fig. 4). Among the larger cells were several multinucleated elements resembling foreign body giant cells. A few mitotic figures were found. Eosinophils and polymorphonuclear leukocytes were rare. The blood vessels contained no excess of lymphocytes. There were no areas of necrosis, hemorrhage, ulceration or thrombosis of the vessels.

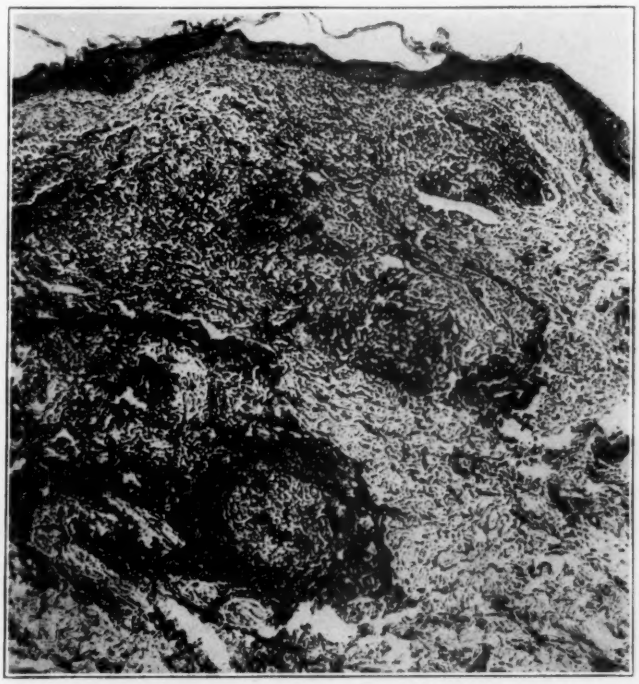

Fig. 2.—Low power view showing the infiltrate in the corium and the lymph follicle appearance of the deep-seated foci.

This case was presented before the Four Cities Dermatological Society on Dec. 10, 1931,[5] at which time Dr. Wile and others were of the opinion that the leukemic infiltrates occurred at the site of a pre-existing zoster. Unfortunately the patient was not seen at the time the original eruption developed, but from the suggestive history and the striking segmental distribution of the papules, in addition to the fact that in the four similar cases in the literature the condition followed zoster, a diagnosis of preexisting herpes zoster seemed tenable.

5. Barney, R. E.: Leukemia Cutis Resembling Herpes Zoster, Arch. Dermat. & Syph. **25**:1150 (June) 1932.

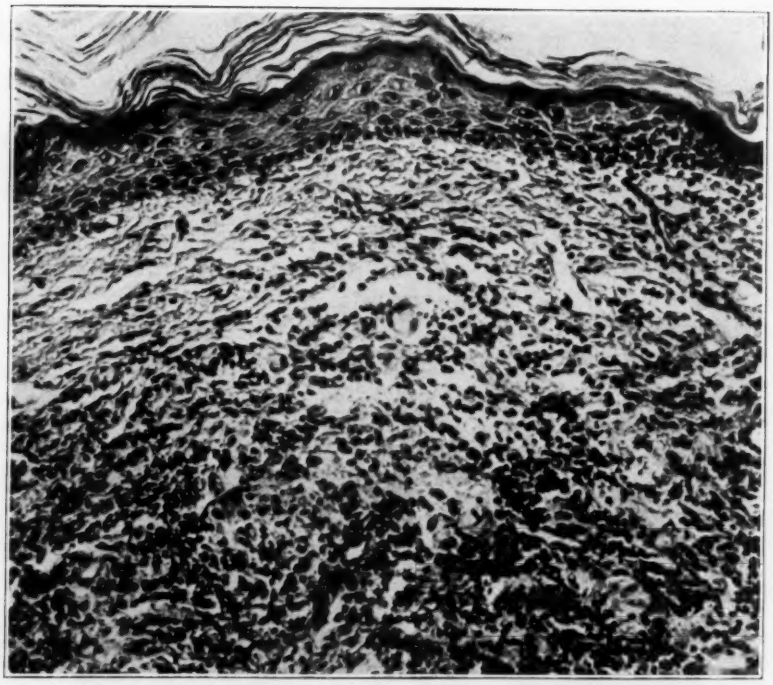

Fig. 3.—Photomicrograph showing the flattened epidermis and the infiltrate in the upper layer of the corium containing a giant cell.

Fig. 4.—Photomicrograph showing a large deep focus resembling a lymph follicle.

Halle,[1] in reviewing the literature up to 1930, was able to collect sixteen cases of herpes zoster associated with lymphatic leukemia, but in only two of these cases were leukemic infiltrates found in the zoster scars. A striking feature of Halle's report was that in eleven of the sixteen cases the zoster was generalized. Freund [6] has attributed the large number of cases of generalized zoster in persons with leukemia to the advanced age of the patients and the lowered resistance produced by the leukemic condition. The more recent literature [7] contains an increasing number of reports of zoster associated with leukemia, which is usually of the generalized type.

The pathogenesis of zoster associated with leukemia has not been definitely settled. The view has been expressed [8] that zoster may be due to a leukemic infiltration of the posterior root ganglions, but the autopsy observations are so few that no definite conclusion can be reached.

Fischl [9] reported a case of generalized herpes zoster, the primary eruption occurring over the distribution of the fifth nerve on the right side. At autopsy both gasserian ganglions revealed periganglionic leukemic infiltration with inflammatory changes inside the ganglions, most marked on the right side. The author could not decide the causal relationship of the leukemic changes to the zoster.

Freund's patient [10] presented gangrenous zoster involving the distribution of the third cervical nerve on the left side, and in addition a generalized vesicular eruption. At autopsy, inflammatory changes were seen in the third cervical ganglion on each side, in the fourth and fifth cervical ganglions on the left side and in the third and fourth

6. Freund, H.: Zoster generalisatus und Leukämie, Dermat. Wchnschr. **88**: 375, 1929.

7. Brandt: Herpes zoster generalisatus und Lymphadenose (2 Fälle), Acta dermat.-venereol. **14**:514, 1933. Arzt: Herpes zoster gangraenosus et generalisatus bei mit Arsen behandelter leukämischer Lymphomatose, Dermat. Wchnschr. **96**:725, 1933. Kalz: Thorakalzoster bei bestehender lymphatischer Leukämie, Zentralbl. f. Haut- u. Geschlechtskr. **44**:622, 1933. Haack, K.: Zoster generalisatus bei lymphatischer Leukämie, Dermat. Wchnschr. **95**:1819, 1932. Proppe, A.: Ueber Erytheme, Dermat. Ztschr. **69**:41, 1934. Zeisler, in discussion on Ormsby, O. S.: Herpes Zoster Associated with a Generalized Varicella-Like Eruption, Arch. Dermat. & Syph. **17**:140 (Jan.) 1928. Skeer, J.: Herpes Zoster Generalisatus: Report of Two Cases Occurring in Patients with Lymphatic Leukemia After Treatment with Roentgen Rays, ibid. **34**:809 (Nov.) 1936.

8. Pusey, W. A.: Principles and Practice of Dermatology, New York, D. Appleton & Company, 1924, p. 269. Becker, S. W., in discussion on Barney.[5] Halle.[1]

9. Fischl, F.: Herpes zoster generalisatus bei Leucaemia lymphatica, Arch. f. Dermat. u. Syph. **118**:553, 1914.

10. Freund, H.: Zoster und Leukämie, Arch. f. Dermat. u. Syph. **154**:476, 1928.

cervical ganglions on the right side as well as in their posterior roots. The second, third and fourth cervical segments of the cord showed the same changes. This relatively widespread type of inflammatory reaction in the nervous system is not unusual in ordinary zoster without leukemia. A hematoma found near the third cervical ganglion, corresponding to the distribution of the primary zoster, was considered a predisposing factor for the localization of the zoster virus.

In the case of generalized zoster reported by Damm,[11] leukemic changes were found in all segments of the spinal cord examined (the seventh cervical segment, the fifth, sixth, seventh, eighth and twelfth thoracic segments and the second and third lumbar segments). The changes were most marked in the lumbar segment corresponding to the distribution of the primary zoster. A diffuse lymphocytic infiltration was also found around the entrance of the posterior roots of the spinal nerves. The spinal ganglions were not examined. The author expressed the opinion that the leukemic changes acted as a predisposing factor for the localization of the zoster virus.

No changes which might be considered specific leukemic manifestations were found in the nervous system in the case recorded by Lynch.[12]

In Wohlwill's patient[13] a leukemic infiltrate was found at autopsy in both trigeminal roots, while examination of the gasserian ganglion gave negative results. Clinically this patient presented a nickel-sized eruption involving the left cheek, which corresponded morphologically to herpes zoster. This was undoubtedly herpes simplex.

The observations made at autopsy on these patients with lymphatic leukemia do not support the view that herpes zoster may be caused by leukemic infiltration in the posterior root ganglions. It is assumed that the leukemic changes produce a locus minoris resistentiae, where the specific zoster virus localizes and multiplies.[14]

SUMMARY

A case of lymphatic leukemia in which there were leukemic infiltrates in the skin of zosteriform arrangement, presumably occurring at the site of preexisting zoster, is reported. A review of the literature shows that this type of case is rare.

11. Damm, P.: Om den aetiologiske sammenhaeng mellem zoster generalisatus, leucaemi og varicellen, Ugesk. f. læger **93**:1279, 1931.

12. Lynch, F. W.: Cutaneous Lesions Associated with Monocytic Leukemia and Reticulo-Endotheliosis, Arch. Dermat. & Syph. **34**:775 (Nov.) 1936.

13. Wohlwill, F.: Zur pathologischen Anatomie des Nervensystems beim Herpes zoster, Ztschr. f. d. ges. Neurol. u. Psychiat. **89**:171, 1924.

14. Cole, H. N.: Personal communication to the author. Dr. Cole has suggested that perhaps in the sense of Milian's nine day erythema, the leukemic infiltrate so lowers the local immunity that opportunity is afforded for the virus of herpes zoster to set up specific changes.

ABSTRACT OF DISCUSSION

DR. H. R. FOERSTER, Milwaukee: I should like to comment briefly on a case that bears some similarity to the one so ably presented by Dr. Barney. In this instance the patient was a previously healthy boy, aged about 16, who was reported to have had a severe attack of varicella. On involution of the varicella eruption his constitutional symptoms increased; he became gravely ill and was hospitalized. A blood count led to a diagnosis of acute lymphatic leukemia; there were no cutaneous lesions. Tissue was removed from the site of a varicella lesion which had undergone involution, and biopsy showed a typical leukemic infiltrate compatible with a histologic diagnosis of leukaemia cutis. Additional tissue was removed from normal skin, and a biopsy of this tissue showed a leukemic infiltrate, but one much less pronounced than that in the first specimen. At the site of the healed lesion the infiltrate was much like that seen in Dr. Barney's case. In the apparently normal skin the infiltrate was confined to the perivascular zones and the cutaneous glands. I believed that the trauma of the varicella inflammation precipitated the leukemic reactions at the sites of previous varicella, or varicella-like lesions, in a patient who already had unrecognized lymphatic leukemia. The latter was activated into a fulminating process by his illness. Unfortunately, the boy died in a few days and it is purely speculative as to what cutaneous developments might have occurred. I believe that in these two patients inflammation from preexisting disease activated latent leukemia and localized the cutaneous leukemic lesions.

DR. H. J. PARKHURST, Toledo: It may be interesting to record the following brief and incomplete case report: In the summer of 1934 a married woman aged 49 was first admitted to the County Hospital in Toledo with chronic lymphatic leukemia which was apparently of at least two years' duration. The patient had taken solution of potassium arsenite for two months, after which a painful outbreak of zoster appeared on her right shoulder, arm and forearm in the region of the third to the sixth cervical nerve, and there were a few disseminated vesicles on the trunk. Numerous transfusions of citrated blood had been given, and the last one, two days before the outbreak of zoster, had been followed immediately by a rise in temperature from normal to 102.4 F. This temperature had subsided to normal in twenty-four hours, and several carious teeth had then been extracted; all of this took place prior to the cutaneous outbreak. Twelve days after the outbreak lesions on the shoulder and arm became gangrenous. The outbreak persisted for six weeks. After this outbreak an ulcerated lesion on the right arm did not heal for over six months. Pink keloid-like patches persisted at the sites of many of the lesions, subsiding slowly after a number of months. At the time I felt that the zoster was probably of arsenical origin, and I regret that a biopsy was not performed. The patient died of lobar pneumonia a year later.

DR. HAMILTON MONTGOMERY, Rochester: Dr. Barney is fortunate in having the opportunity to demonstrate a true leukemic infiltrate in herpes zoster. As a rule herpes zoster with lymphoblastoma reveals histologically a nonspecific type of infiltrate. Emphasis must be placed on the frequent occurrence of herpes zoster in all types of lymphoblastoma, especially in Hodgkin's disease. In the case of elderly persons especially one must keep in mind that herpes zoster may frequently be an early indication of cutaneous or systemic lymphoblastoma.

DR. H. N. COLE, Cleveland: I saw this patient of Dr. Barney's and was very much interested in the case. Dr. Driver and I had an opportunity to see a similar patient with probable Hodgkin's disease, in whom herpes zoster with infiltrate developed later. Unfortunately, the patient lived out of town and we knew

nothing of his death; autopsy was not performed. This type of case is extremely interesting and rare, but if watched for closely by dermatologists, more such cases might be encountered.

Dr. Harther L. Keim, Detroit: I do not think it is necessary to look for a leukemic infiltrate in cord ganglions to explain the zosteriform leukemic eruption in the case described by Dr. Barney. It is well known that trauma, friction or some other minor injury often determines the site of a true nodular infiltrate. An observation made some years ago in a study of leukaemia cutis would seem to have some bearing on the factors producing this zosteriform leukemic eruption. Biopsy specimens of clinically uninvolved skin of patients with lymphatic leukemia revealed microscopic infiltrates varying from definite small masses of lymphatic cells to the well defined bandlike infiltrate in the upper part of the cutis. If the skin of Dr. Barney's patient contained such microscopic infiltration, the inflammatory reaction produced by the herpetic lesion might readily result in such an outpouring of lymphatic cells as to produce true leukemic infiltrates along the course and distribution of a simple herpes zoster.

QUININE BISULFATE AS A DESENSITIZING AGENT IN TREATMENT OF LUPUS ERYTHEMATOSUS

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AND
A. R. BIRT, M.D.
WINNIPEG, CANADA

Eighty-nine cases of lupus erythematosus under observation in the outpatient department of the Winnipeg General Hospital have been investigated. Of this number, six were instances of the acute disseminate type and are not considered in this paper.

A study of the incidence according to sex showed 60 per cent of patients to be female.

A tabulation according to age showed the disease to have a marked predilection for the third and the fourth decade, approximately two thirds of the patients falling into that age group (fig. 1). There was no patient under 10 years of age. Some of the older patients had had the disease in mild form for many years but did not seek treatment.

A study of the seasonal incidence was particularly interesting. Figure 2 shows the month of onset in forty-seven cases.

CLASSIFICATION OF TWENTY-NINE PATIENTS WITH LUPUS ERYTHEMATOSUS ACCORDING TO INDICATIONS OF TUBERCULOSIS

In twenty-nine of the eighty-three cases of lupus erythematosus in this series thorough investigation was made for tuberculosis. The history was carefully taken; physical examination was made; a roentgenogram of the chest was obtained, and a tuberculin test was performed. In nineteen of the twenty-nine cases thus studied there were one or more positive findings. In ten there was no evidence of tuberculosis. Patients with no sign of tuberculosis will be designated, for convenience, as group 1 and those with one or more positive findings as group 2. The remaining fifty-four patients were not investigated for manifestations of tuberculosis.

Six of the patients in group 2 had had tuberculosis, while five had been exposed to the disease. Physical examination revealed enlargement of the lymph nodes of eight patients. A roentgenogram of the

Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 3, 1937.

chest showed definite evidence of tuberculosis for five. Mantoux tests were done for seventeen patients. Sixteen had positive reactions with a dilution of 1 : 1,000 of old tuberculin.

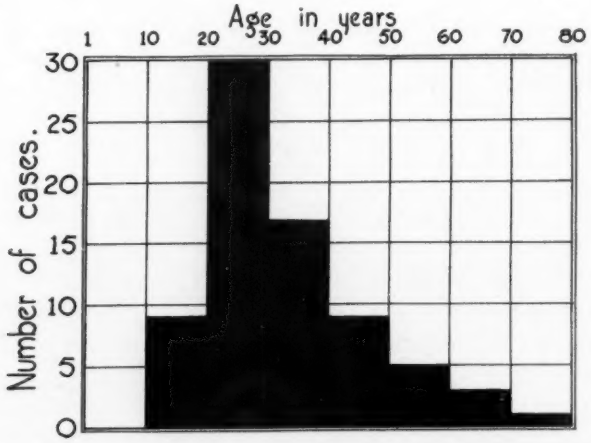

Fig. 1.—Incidence according to age in seventy-four cases of the discoid type of lupus erythematosus.

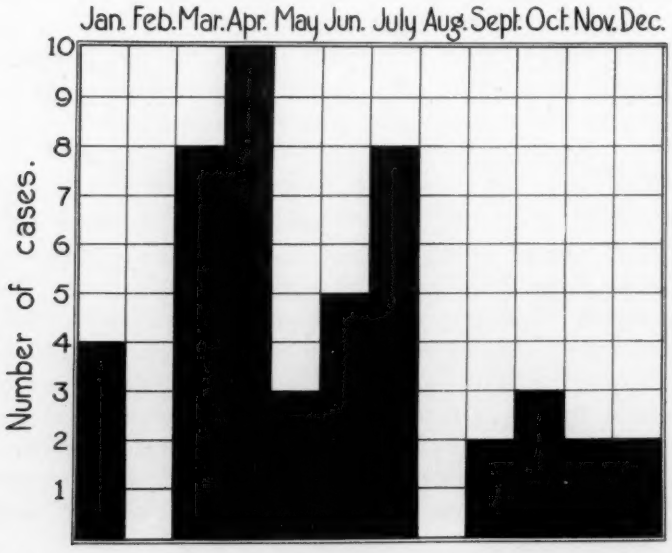

Fig. 2.—Seasonal incidence in forty-seven cases of lupus erythematosus.

The groups had certain features in common. The incidence according to sex was practically the same in both, there being, roughly, 65 per cent female and 35 per cent male patients. The average age in group 1 was 23 years, and in group 2 it was 25 years. Approximately the same

proportion of patients of each group suffered from exposure to light and change in temperature, 55 per cent of the first group being so affected and 60 per cent of the second.

CLINICAL APPEARANCE OF PATIENTS OF GROUP 1

The patients of group 1 had lesions situated chiefly on the bridge of the nose, the cheeks and the ears. Occasionally lesions were found on the forehead, the eyelids, the lips and the scalp. The eruption was composed of erythematous plaques with irregular, deeper-colored borders, and they were surmounted by a fine, adherent gray scale. The scales, when removed, had small spines on their under-surfaces which dipped down into the distended sebaceous follicles. The lesions healed, leaving a scarcely visible fine white scar.

CLINICAL APPEARANCE OF PATIENTS OF GROUP 2

A wider range of lesions was found among patients of group 2. There were those of the erythematous type already described in group 1 and another type which might be called the scaly type of lesion. The distribution of the eruption was essentially the same as among patients in group 1. The erythema was fainter and the lesions flatter. They were covered by thick, adherent white scales with stalactite-like processes from the under-surface. They left deep-set papery scars in healing.

The incidence of lesions of the two types among the patients of group 1 and of group 2 was as follows:

Group	Number of Patients	Type of Lesion	
		Erythematous	Scaly
1	10	10	0
2	19	15	4

During classification of the lesions in the two groups it was noted that Mr. S. had typical scaly lesions on both cheeks. His family history, a physical examination and a roentgenogram of his chest gave no evidence of tuberculosis. The routine intradermal tuberculin test had been omitted. Thus he apparently belonged in group 1 and had a scaly type of lesion. All the other scaly lesions affected patients in group 2. The patient was located, and a tuberculin test was done. The result was 3 plus. The suggestion is offered that the scaly type of lesion of lupus erythematosus is invariably associated with a positive reaction to tuberculin.

TREATMENT

In the present series of cases quinine sulfate was given internally, and protective ointments and lotions were used locally. The quinine salt was given to the limit of tolerance in 5 grain (0.325 Gm.) tablets, three times a day after meals. If any signs of cinchonism developed the

dose was decreased. The results obtained by this medication were as follows:

Group	Clinically Cured	Unimproved	Lost From Observation
1	8	0	2
2	11	5	3

An investigation of the five patients in group 2 who showed no improvement revealed that one patient had an idiosyncrasy to quinine and the other four had the scaly type of lesion. The eleven patients who experienced clinical cure had lesions of the erythematous type. Thus, of the twenty-four patients for whom the results of treatment are known, nineteen were cured. Of the twenty patients with the erythematous type of lesion, nineteen were cured and one did not tolerate quinine.

The remaining fifty-four patients were not as thoroughly examined for tuberculosis as the twenty-nine described in groups 1 and 2. Thirty-three, however, were given treatment with quinine. In all cases in which the disease was in the erythematous stage improvement was noted. Lesions of the scaly type did not respond to quinine therapy and were treated by other methods.

COMMENT

In this study an effort was made to establish clinically what bearing tuberculous infection has on lupus erythematosus. As previously mentioned, classification of seventy-four patients according to age showed that two thirds of them were in the second or the third decade. This is the period in which, according to Tidy,[1] tuberculosis has its highest mortality.

It is difficult to assay the value of reaction to tuberculin in these cases. Forman [2] said: "A positive tuberculin reaction produced by intradermal inoculation has been accepted as evidence of tuberculous infection with sensitization of the skin." Owing to the endemic character of tuberculosis and the relatively high percentage of positive reactions to tuberculin reported in some centers, such a reaction must not be stressed too much in searching for the cause of any disease. If, however, the number of positive results obtained in a series of cases such as this is relatively higher than those obtained in a similar group of apparently healthy persons of approximately the same age, then it is reasonable to suppose that the increased sensitivity of the skin to tuberculin has some relation to the cause of the disease. Of this series of cases,

1. Tidy, H. Letheby: A Synopsis of Medicine, ed. 5, Baltimore, William Wood & Company, 1930.

2. Forman, Louis: On the Aetiology of Erythema Nodosum, Brit. J. Dermat. **48**:123, 1936.

in 65 per cent of the group in which careful examination was made there was either a positive reaction to tuberculin or some other evidence of tuberculosis. There was a positive reaction to tuberculin in 61 per cent. Dr. D. L. Scott, of the Central Tuberculosis Clinic, Winnipeg, Canada, furnished for comparison the results of a series of tuberculin tests of 360 nurses who were just commencing training. Their average age was 20 years, which is about the same as the average age of the patients with lupus erythematosus in our group.

The geographic distribution in the two series was the same. Most of the nurses, as well as the patients, lived in Manitoba or Saskatchewan. There was an almost equal division between urban and rural residents. Of the 360 nurses tested, 112, or 31 per cent, gave a positive reaction to tuberculin. Though the nurses may be regarded as a select group physically, it does not account for the fact that twice as many of the patients gave a positive reaction to tuberculin.

Dr. Daniel Nicholson, of the University of Manitoba Faculty of Medicine, furnished the results of a second control series of tuberculin tests of fourth year medical students. All the subjects were in their second clinical year, and most of them had spent several weeks at a sanatorium for tuberculous patients. Their average age was 25.5 years, and their homes were similar to those of the two preceding groups. Of 142 students tested, 97, or 68 per cent, had positive reactions to tuberculin. This increase in positive reactions to tuberculin may be accounted for in two ways: (1) by the increased age of the group and (2) by the greatly increased chance of exposure to tuberculosis.

It does not seem reasonable that the percentage of positive reactions to tuberculin should more than double in five years unless some factor other than the patient's increased age is involved. It is far more probable that the great increase in positive results obtained among medical students was due to greatly increased exposure to tuberculosis. Until more tests are done on normal subjects, little or no weight can be attached to the tuberculin test in searching for the cause of any abnormal condition of the body. However, the percentage of positive reactions to tuberculin in the group of medical students and the series of patients tested is probably high for persons living in Canada. In the one group it may have been due to increased exposure to tuberculosis at work and in the other to a definite part that tuberculosis plays in the causation of the disease.

It has often been suggested that exposure to sun and wind or sudden changes in temperature may precipitate an attack of lupus erythematosus. Of this series of eighty-three cases, there was such a history in thirty-two. Twenty-seven patients stated that they had experienced ill effects from exposure to the sun or other forms of ultraviolet light. The ultraviolet band in sunlight is thought to affect the sensitizing sub-

stance in the patients' skin. This contention is supported by the seasonal incidence in the forty-seven cases recorded in figure 2. The period from the first of March to the end of July embraces the onset in almost two thirds of the cases. This is the period in which ultraviolet radiation reaches its maximum in this country.

The following case supports this view:

Mrs. J. W., a housewife aged 21, was first examined in May 1931. She was treated at that time for tuberculous adenitis, involving both posterior cervical chains of glands. Roentgenograms of her chest revealed calcareous changes in the apexes and roots of both lungs. There was no evidence of active tuberculous infection in the chest. An intradermal tuberculin test gave positive results. Roentgen therapy to the glands of the neck and generalized treatment with the quartz lamp were given. Within two weeks typical erythematous scaly lesions of lupus erythematosus developed on her face. Treatments with the quartz lamp were discontinued, and quinine sulfate was given by mouth. The lesions improved till the following February, when, unfortunately, she was given a second course of treatments with the quartz lamp. There was an immediate relapse of the eruption. At that time she had, in addition, typical papulonecrotic tuberculid on the extremities.

Ultraviolet radiation was an apparently necessary factor in the causation of the disease. Lupus erythematosus developed in a definitely tuberculous patient who later had a recognized tuberculous eruption in the form of papulonecrotic tuberculid.

Because of the part played by ultraviolet radiation in the causation of lupus erythematosus, the possibility that quinine might in some way change the reaction of the skin to the rays suggested itself. A series of quinine salts was prepared, and the specimens were examined under filtered (Wood's) ultraviolet rays in a darkened room. Quinine sulfate and quinine hydrochloride were the only two salts examined that did not fluoresce brightly. The double salts of these drugs—that is, quinine bisulfate and quinine dihydrochloride—fluoresced much more brilliantly than any others examined.

Therefore quinine bisulfate has been substituted for quinine sulfate in these cases. We believe that the desensitization of the skin by the action of the quinine accounts for the greater percentage of clinical cures.

CONCLUSIONS

1. Quinine sulfate is of great value in the treatment of the erythematous stage of lupus erythematosus.

2. It is particularly valuable in the erythematous stage, when the tuberculin reaction is negative.

3. Quinine bisulfate is more efficient than quinine sulfate, on account of its greater desensitizing power.

ABSTRACT OF DISCUSSION

DR. MARION B. SULZBERGER, New York: I enjoyed Dr. Davidson's paper and think it is timely again to bring to attention the use of quinine for the treatment of lupus erythematosus, especially when the many cases in which the condition resists therapy with a gold compound and the many grave dangers sometimes accompanying the injection of gold salts are considered. In view of this report, perhaps the early use of quinine will be more frequent and the use of gold salts delayed. The deleterious effect of light has, of course, been proved in many cases of lupus erythematosus, and I wonder whether the quinine, even by ingestion, may not act as a filter. This drug is one of the best absorbers of light. I have often used quinine not only internally but in combination with phenyl salicylate and tannic acid externally in lupus erythematosus. In many instances I have had satisfactory results.

I wish to ask what concentration of tuberculin Dr. Davidson has employed in determining the classification of patients according to the reaction to tuberculin.

DR. GEORGE C. ANDREWS, New York: One type of quinine salt has been used recently in cases of acute disseminated lupus erythematosus with some benefit. I think the benefit is sufficient to make it worth mentioning. It is the quinine bismuth iodide tartrate put out under the trade name of tartro-quiniobine. A patient under my care who was suffering from acute disseminated lupus erythematosus was sick and greatly depressed. The condition did not respond to anything done for her, including rest in bed, until during the past five or six weeks, when she has been given injections of this drug, which apparently has caused definite improvement.

DR. E. WILLIAM ABRAMOWITZ, New York: The use of quinine for the treatment of lupus erythematosus has been revived recently, but it is not being used as originally indicated by Höllander. He suggested that tincture of iodine be applied locally ten minutes after ingestion of 0.5 Gm. of quinine hydrochloride twice daily. The effects were attributed to the local liberation of nascent iodine. It is stated by some authorities that quinine administered internally may act as a sensitizing agent to light. It is known that gold compounds may act similarly. Yet these preparations have proved effective in clearing up lesions of lupus erythematosus, although sensitization to light is characteristic of the disease.

DR. ROBERT L. GILMAN, Philadelphia: I know Dr. Davidson did not have time to elaborate and give details, but I should like to know over how long a period the quinine was used, whether he found any cases in which it was contraindicated and whether any studies were made of the effect of quinine on the leukocytes.

DR. A. M. DAVIDSON, Winnipeg, Canada: I wish to thank the discussers and to state that my idea about the fluorescence is that it does act as a protective agent, because I tested these substances with ultraviolet radiation and Wood's filter. We tested a small series and found that the double salts fluoresce much more brilliantly and absorb much more light than the others.

In answer to Dr. Gilman: The average period of treatment was between ten and eleven weeks with quinine bisulfate in doses of 5 grains (0.325 Gm.) three times daily. We found only one patient who was sensitive to the quinine, and that patient had an acute reaction after one dose. No studies were made of the effect on the leukocytes.

ARTIFICIAL FEVER AS AN ADJUNCT IN THE TREATMENT OF NEUROSYPHILIS

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Artificial fever, induced either by the inoculation of malarial parasites or by various physical agents, has become an integral part of the management of neurosyphilis. Malarial therapy was introduced by Wagner-Jauregg [1] for the treatment of dementia paralytica in 1918. Many later reports [2] indicated that the production of fever was of distinct value in treating not only dementia paralytica but other types of neurosyphilis. Subsequently other methods of inducing artificial fever were introduced, including inoculation with the parasites of rat bite fever and of relapsing fever; injection of vaccines, such as bacterial vaccine made from the typhoid bacillus and the paratyphoid A and B bacilli; injection of sulfur in oil and methods that used physical means alone, such as diathermy, radiothermy, the use of inductotherm, electric blankets, hot baths and heat cabinets such as the Kettering hypertherm and a simplified procedure called the "blanket method." The "blanket method" [3] was employed in treatment of the series of patients reported on in this paper. The therapeutic results obtained by the various methods used to induce fever appear to be comparable, provided the temperature

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From the Department of Dermatology of the Division of Medicine of the University of California Medical School and the Department of Dermatology of Mount Zion Hospital.

1. Wagner-Jauregg, Julius: Ueber Einwirkung der Malaria auf die Progression Paralyse, Psychiat.-neurol. Wchnschr. **20**:132, 1918.

2. (*a*) Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933. (Reviews the recent literature on malaria therapy.) (*b*) Wile, U. J., and Hand, E. A.: Ten Years' Experience with Malaria in Neurosyphilis, Am. J. Syph., Gonor. & Ven. Dis. **20**:630 (Nov.) 1936. (*c*) Solomon, H. C., and Epstein, S. H.: General Paresis: Treatment by Tryparsamide-Induced Fever Sequence, ibid. **20**:281 (May) 1936. (*d*) Neymann, C. A.: The Treatment of Disease by Electropyrexia, Proc. Roy. Soc. Med. **29**:151 (Dec.) 1935. (Reviews literature on treatment of general paresis by electropyrexia.) (*e*) Dennie, C. C.; Polsky, M., and Semoine, A. N.: Hyperpyrexia Produced by Hot Bath in the Treatment of Syphilis, J. Missouri M. A. **33**:1 (Jan.) 1936. (*f*) Simpson, W. M.: Artificial Fever Therapy of Syphilis and Gonococcic Infections, New York State J. Med. **36**:1290 (Sept. 15) 1936.

3. Epstein, N. N.: The Blanket Method of Inducing Artificial Fever, Arch. Phys. Therapy **78**:199 (April) 1937.

is elevated to a sufficient height and maintained for a sufficient period. Krusen,[4] in a paper on the present status of artificial fever therapy, has reviewed the recent literature on this subject.

The forms of neurosyphilis in which artificial fever is used have been extended to include not only dementia paralytica but the tabetic form of dementia paralytica, tabes dorsalis and all other types that prove resistant to drug therapy. At present the greatest good can be done the patient with neurosyphilis by combining chemotherapy, including the use of tryparsamide, the arsphenamines and bismuth, with some form of fever therapy.

The induction of artificial fever by physical means has several advantages over the use of biologic agents, particularly for the patient who does not require institutional care. Among these advantages are: (1) that these methods are more readily available and the fever induced by them more easily controlled; (2) that antisyphilitic chemotherapy can be administered simultaneously with fever therapy so induced; (3) that less drain on the patient's finances is necessary, and (4) that fever induced by physical methods has little debilitating effect on the patient.

It is my purpose in this paper not to discuss the relative merits of the various methods of inducing artificial fever but rather to report the clinical and serologic findings in a group of patients with the various forms of neurosyphilis who were treated by artificial fever produced by the blanket method together with chemotherapy.

CLINICAL STUDY

The series reported includes a total of eighty-seven patients, sixty of whom were male and twenty-seven female. The average age was 40.7 years. All these patients were in the late phase of syphilis, with evidence of involvement of the central nervous system (table 1).

OBSERVATION PERIOD

The periods of observation of the patients with various forms of neurosyphilis (table 2) have been divided into two phases, i. e., the number of months before and the period after fever therapy was instituted.

The average total period of observation was thirty-seven and seven-tenths months, or slightly over three years. All the patients were followed carefully and examined at stated intervals. Examination of table 2 shows that the condition had been somewhat resistant to drug therapy, as fever therapy was not introduced for an average of over one and a half years after chemotherapy had been started. In one group,

4. Krusen, F. H.: The Present Status of Fever Therapy Produced by Physical Means, J. A. M. A. **107**:1215 (Oct. 10) 1936.

fever therapy was not used until the patients had been given drug therapy for an average of almost two and a half years.

DRUG THERAPY

Drug therapy was administered to all patients throughout the period of observation and consisted mainly of the use of tryparsamide and of bismuth subsalicylate. Neoarsphenamine was employed to a less extent, some patients, particularly those with asymptomatic neurosyphilis or meningovascular syphilis, receiving a moderate amount. A few patients received mercury in the form of mercuric succinimide or mercuric salicylate. In all cases drug therapy was administered simultaneously

TABLE 1.—*Classification of Patients*

Diagnosis,	Number of Patients	Male	Female	Average Age, Years
Dementia paralytica	17	14	3	41.2
Tabetic form of dementia paralytica	17	13	4	41.6
Tabes dorsalis	23	17	6	44.6
Asymptomatic neurosyphilis	20	11	9	40.0
Meningovascular syphilis	10	5	5	36.3
Total	87	60	27	40.7

TABLE 2.—*Average Observation Period in Months*

Diagnosis	Before Fever Therapy	After Fever Therapy	Total
Dementia paralytica	19.0	13.0	32.0
Tabetic form af dementia paralytica	18.4	20.5	38.9
Tabes dorsalis	23.5	23.2	46.7
Asymptomatic neurosyphilis	29.0	18.0	47.0
Meningovascular syphilis	8.6	15.3	23.9
Average	19.7	18.0	37.7

with the fever therapy. No effort was made to limit medication to any particular drug during the period of fever therapy. Table 3 shows the amount of tryparsamide and of bismuth subsalicylate that were given.

FEVER THERAPY

Fever therapy was administered to all the patients in the series. An effort was made to give each patient a series of ten weekly treatments, each consisting of five hours at a temperature of approximately 40 or 40.5 C. (104 or 105 F.). No patient is included in this series who did not receive at least four treatments totaling twenty hours. The number of hours of fever for the entire group of eighty-seven patients was 4,720, or an average of 54.2 hours for each patient. Four patients had received malaria therapy previously, but results had not been satisfactory.

Fever therapy was given as promptly as possible to the patients with dementia paralytica or the tabetic form of dementia paralytica. It was given to the patients with tabes dorsalis when drug therapy had failed to influence the symptoms of pain, crisis, ataxia or failing vision and when the spinal fluid had not responded well. For the groups of patients with asymptomatic neurosyphilis and meningovascular syphilis, fever therapy was instituted after the administration of drugs for an average of twenty-nine months and of eight and six-tenths months respectively.

METHOD

The artificial fever was produced by wrapping the patients in bath blankets, large woolen blankets and then rubber and canvas sheeting. The initial rise in temperature was accelerated by placing a common body frame containing twelve carbon lights over the patient. Warm fluids containing salt and sugar were given during the treatments and morphine was administered to combat restlessness. The details of the technic of this method, which I call the "blanket method," with a complete discussion of the indications, contraindications, dangers and effects of artificial fever, have been published recently. The procedure of fever therapy was conducted in every instance within the hospital by a staff of nurses thoroughly trained in the technic and with the house staff in constant attendance. Each treatment required twenty-four hours' hospitalization, after which the large majority of patients were able to return to their usual occupations. Artificial fever produced by this method was found to have little debilitating effect on the patient.

TABLE 3.—*Drug Therapy*

Diagnosis	Tryparsamide, Gm.		Bismuth Subsalicylate, Gm.	
	Number of Cases	Total Average Dose	Number of Cases	Total Average Dose
Dementia paralytica	16	95.6	14	10.6
Tabetic form of dementia paralytica	15	100.2	17	9.8
Tabes dorsalis	16	72.0	22	11.7
Asymptomatic neurosyphilis	15	99.0	20	11.9
Meningovascular syphilis	9	54.2	10	6.9

SEROLOGIC RESULTS

The spinal fluid of each patient was examined before and after fever therapy. A total of 278 examinations of the spinal fluid were made for the entire series of eighty-seven patients, or an average of 3 per patient. The Wassermann reaction of the spinal fluid was found to be negative before fever therapy was given for two patients with tabes dorsalis and strongly positive for the remaining eight-five patients. Table 4 shows the effect of therapy on the Wassermann reaction of the spinal fluid.

The most striking effect on the spinal fluid was found in tabes in which the Wassermann reaction of approximately 74 per cent of the

patients was rendered negative and that of an additional 4.3 per cent less strongly positive. The patients with asymptomatic neurosyphilis experienced good responses, the reactions of the spinal fluid of 70 per cent becoming negative, whereas improvement was noted in the fluid of 15 per cent. The reaction of the spinal fluid of 60 per cent of the patients with meningovascular syphilis became negative and that of 10 per cent less positive. The response in dementia paralytica was

TABLE 4.—*Wassermann Reactions of the Spinal Fluid*

		Changed from						Remained			
		Positive to Negative		Positive to Less Positive		Positive to More Positive		Positive		Negative	
Diagnosis	Number of Cases	No.	%	No.	%	No.	%	No.	%	No.	%
Dementia paralytica	17	8	47.0	5	29.4	4	23.5	..	....	..	....
Tabetic form of dementia paralytica	17	5	29.4	4	23.5	2	11.8	6	35.3	..	....
Tabes dorsalis	23	17	73.9	1	4.3	..	....	3	13.0	2	8.6
Asymptomatic neurosyphilis	20	14	70.0	3	15.0	..	....	3	75.0	..	....
Meningovascular syphilis	10	6	60.0	1	10.0	..	....	3	30.0	..	....
Total	87	50	57.4	14	16.0	6	6.85	15	17.0	2	2.3

TABLE 5.—*Colloidal Gold Curve*

		Changed to						Remained			
		Normal		Less Abnormal		More Abnormal		Normal		Abnormal	
Diagnosis	Number of Cases	No.	%	No.	%	No.	%	No.	%	No.	%
Dementia paralytica	17	5	29.4	8	47.0	..	....	..	....	4	23.5
Tabetic form of dementia paralytica	17	2	11.8	12	70.5	1	5.9	..	....	2	11.8
Tabes dorsalis	23	13	55.9	1	4.3	..	....	2	8.6	7	30.1
Asymptomatic neurosyphilis	20	14	70.0	3	15.0	..	....	2	10.0	1	5.0
Meningovascular syphilis	10	5	50.0	4	40.0	..	....	..	....	1	10.0
Total	87	39	44.8	28	32.1	1	1.14	4	4.5	15	17.0

better than that in the tabetic form of dementia paralytica. The reaction of the spinal fluid became negative in 47 per cent of cases of the former condition and showed improvement in 29.4 per cent, while of cases of the latter, negative results were obtained in 29.4 per cent and less positive reactions in 23.5 per cent.

It was found considerably more difficult to render normal the colloidal gold curve than the Wassermann reaction of the spinal fluid. In many instances the colloidal gold curve showed minimal changes in the midzone when the rest of the spinal fluid had become normal. However, the colloidal gold curve either became normal or improved in sixty-seven cases, or 77 per cent.

CELL COUNT AND PROTEIN CONTENT IN THE SPINAL FLUID

For 94.7 per cent of those patients with abnormal cell counts at the institution of fever therapy the cell count was reduced to 6 or less. The cell counts had varied from 258 to normal before treatment was instituted.

Of fifty-four patients for whom studies of the protein and the globulin content of the spinal fluid were made, these were reduced to normal in seventeen, or 31.4 per cent, and reduced but not to normal in twenty-three, or 42.5 per cent.

TABLE 6.—*Serologic Reactions of the Blood*

		Wassermann Test				
		Changed from			Remained the Same	
Diagnosis	Number of Cases	Positive to Negative	Positive to Less Positive	Positive to More Positive	Positive	Negative
Dementia paralytica	11	6	1	1	2	1
Tabetic form of dementia paralytica	11	5	2	..	3	1
Tabes dorsalis	19	9	3	..	5	2
Asymptomatic neurosyphilis	17	7	2	1	3	4
Meningovascular syphilis	7	3	1	..	2	1
Total	65	30 (46%)	9 (13.8%)	2 (3%)	15 (23%)	9 (13.8%)

		Kahn Test				
		Changed from			Remained the Same	
Diagnosis	Number of Cases	Positive to Negative	Positive to Less Positive	Positive to More Positive	Positive	Negative
Dementia paralytica	11	4	..	..	4	3
Tabetic form of dementia paralytica	9	1	1	..	4	3
Tabes dorsalis	18	6	2	1	5	4
Asymptomatic neurosyphilis	15	6	1	2	2	4
Meningovascular syphilis	7	3	1	..	2	1
Total	60	20 (33.3%)	5 (8.3%)	3 (5%)	17 (28.3%)	15 (25%)

The cell count was found to be the element of the spinal fluid most easily affected and was reduced to normal by a relatively short course of drug or fever therapy.

CHANGES IN SEROLOGIC REACTION OF THE BLOOD

Table 6 shows the changes which occurred in the Wassermann and Kahn reactions of the blood in the sixty-five cases in which these tests were carefully checked. The serologic reaction of the blood reversed less readily than did that of the spinal fluid.

RELAPSE OF SEROLOGIC FINDINGS

Serologic relapse of the spinal fluid was noted in two cases. These are presented in detail:

CASE 1.—A. Y., a man aged 28, was first seen in the outpatient department of the University of California in March 1929. In 1927 he had had lesions of secondary syphilis and had received antisyphilitic therapy for one year. When he entered the hospital the Wassermann reaction of his blood was found to be strongly positive. He was treated with neoarsphenamine, a bismuth preparation and mercury for three years. In January 1932 the spinal fluid gave a strongly positive reaction. The patient was given artificial fever for forty hours in March 1932. In August 1932 the reaction of the spinal fluid had become negative. Drug treatment was discontinued until October 1934, when there were strongly positive Wassermann and Kahn reactions of the blood and a strongly positive reaction of the spinal fluid. Fever therapy and medication with tryparsamide and bismuth

TABLE 7.—*Serologic Relapse in Case 1*

Blood			Spinal Fluid				
Date	Wassermann Test	Kahn Test	Date	Wassermann Test	Colloidal Gold Curve	Protein	Cells
March 1929	++++		Jan. 1932	++++	1343100000	+	52
May 1930	Negative	Negative	July 1932	Negative	0000000000	+	1
Sept. 1930	++++	++++	June 1933	Negative	0000000000	—	0
Aug. 1931	Negative	+	Oct. 1934	++++	0123321000	+	23
Sept. 1932	Negative	++++	Nov. 1936	Negative	0122110000	+	3
July 1933	Negative	Negative					
Oct. 1934	++++	++++					
Nov. 1936	Negative	Negative					

TABLE 8.—*Serologic Relapse in Case 2*

Blood			Spinal Fluid				
Date	Wassermann Test	Kahn Test	Date	Wassermann Test	Colloidal Gold Curve	Protein	Cells
Feb. 1931	++++		May 1933	++++			
May 1933	Negative		March 1934	Negative			
Nov. 1933	Negative		Nov. 1935	++++	0000000000	+	29
April 1934	+		Feb. 1937	++++	0001210000	..	45
Jan. 1935	+++						
Aug. 1935	++						
Nov. 1935	+++						
Feb. 1937	++++						

were again used, and reversal of the reactions of the blood and spinal fluid occurred two years later.

CASE 2.—G. S., a man aged 49, was referred to the outpatient department of the University of California in June 1933 for fever therapy. The Wassermann reaction of the blood had been found positive in February 1931, after which he had been given intensive antisyphilitic treatment for two years. In May 1933 the Wassermann reaction of his blood was negative, but that of the spinal fluid was strongly positive.

In June 1933 fever was induced for forty hours. No further antisyphilitic therapy was given except an occasional injection of a bismuth preparation. In March 1934 the reaction of the spinal fluid was negative. In February 1937, when the patient returned to the outpatient department, he was found to have a strongly positive Wassermann reaction of the blood and of the spinal fluid. He was given fifty hours of fever therapy and ten injections of tryparsamide, 2 Gm. each. Drug therapy is being continued.

The serologic relapse of these two patients were strikingly similar. The reactions of the spinal fluid of both had become negative a few months after fever therapy, only to become positive again a few months later. Both patients had voluntarily discontinued drug therapy after the fever therapy. The importance of adequate drug therapy after fever therapy is well illustrated by these two cases.

CHANGES IN CLINICAL STATUS

Dementia Paralytica.—The clinical response in cases of dementia paralytica was satisfactory. The best results were obtained in the cases in which the serologic reactions of the spinal fluid became normal, although in several of the cases in which the changes in the spinal fluid

TABLE 9.—*Clinical Results in Dementia Paralytica*

Complete Remission	Moderate Improvement	Slight Improvement	No Improvement	Total Cases
7	5	3 (1 died of unrelated condition)	2	17

TABLE 10.—*Clinical Results in the Tabetic Form of Dementia Paralytica*

Excellent	Moderate Improvement	Slight Improvement	No Improvement	Total Cases
8	4	4 (1 institutionalized)	1 (Institutionalized)	17

were not marked considerable clinical improvement was noted. Seven patients obtained complete clinical remissions; five others showed moderate improvement and were able to support themselves, mental deterioration apparently having been arrested; three patients showed slight improvement (one of these died of an unrelated condition, and one is alive at present, eight years after a diagnosis of dementia paralytica was made); one patient made no progress, and one became worse, requiring institutionalization.

Tabetic Form of Dementia Paralytica.—An excellent clinical response was noted in eight patients. In five of these the results of serologic tests paralleled the clinical results; in two patients there was no change, while in one a moderate improvement occurred in the spinal fluid. Cessation of convulsive seizures, relief of lightning pains, improvement in gait and ability to resume a gainful occupation were the criteria which served as a guide in the evaluation of the clinical response. Four patients showed moderate improvement; four showed slight improvement; and the condition of one became worse. Of the entire group,

two required institutionalization. Two patients having atrophy of the optic nerve obtained no relief from this condition.

Tabes Dorsalis.—The clinical response did not parallel the serologic response. Reversal of the reaction of the spinal fluid was not always accompanied by symptomatic relief. The clinical result was considered excellent in eight patients; moderate clinical improvement was noted in six; there was slight improvement in four; and no relief of symptoms was experienced by six. Pains of various types, mainly shooting, were noted by eighteen patients. All these patients had complete or partial relief of pain during the period of fever therapy. This relief was permanent in eight patients, while in the rest the pains recurred after weeks or months to a greater or less extent. It was seldom necessary to administer narcotics to any of this group of patients treated by this method. Some decrease in ataxia was noted in five patients; in none, however, was the gait restored to normal. Atrophy of the optic nerve occurred in four patients; no improvement was observed. Urinary symptoms improved in two cases. Atrophy of the optic nerve was present in six of the entire series of eighty-seven patients—in none of these was that manifestation benefited by treatment.

Meningovascular Syphilis.—Of the ten patients in this group, three were asymptomatic. The remaining seven experienced marked improvement in general health. The most common symptoms were headache, vertigo and nervous irritability. Two of the patients in this group had congenital syphilis; one, who had frequent convulsive seizures, showed moderate improvement, while the other improved markedly in general health. Residual hemiplegia in one patient was unaffected.

COMMENT

The combined use of chemotherapy and artificial fever therapy has given excellent results in a series of patients with neurosyphilis. The clinical effects and the changes in the serologic findings of the spinal fluid compare favorably with the results obtained by other methods of treatment. It is recognized that in the evaluation of therapeutic results obtained in the treatment of neurosyphilis several factors must be taken into consideration. Among these are the duration of the disease, the response of the individual patient and the extent of the damage done by the infection. It is obvious that the end-results in patients in whom dementia paralytica has produced severe deterioration could not be satisfactory, regardless of the type of therapy used. On the other hand, brilliant therapeutic results may be obtained in patients who have suffered little destruction of the parenchymatous tissue. This fact undoubtedly accounts for occasional conflicting reports found in the literature.

The effects of the method of treatment described here on asymptomatic neurosyphilis are of interest. This condition had usually been resistant to drug therapy, most patients having been under observation for an average of twenty-nine months before fever therapy was instituted. This indicates that fever therapy was an important factor in rendering the Wassermann reaction of the spinal fluid negative in 70 per cent of this group. However, since a large percentage of patients with this type of neurosyphilis respond well to drug therapy alone, fever therapy should not be employed unless the response to drugs is not satisfactory.

The occurrence of serologic relapse in two patients indicates the importance of giving adequate drug therapy after fever therapy. In the treatment of neurosyphilis too much reliance should not be placed on a single method of attack; rather the patient should be given the benefit of the combined use of drugs and artificial fever in adequate amounts.

The artificial fever produced in this group of patients was induced by simple physical means. The therapeutic results obtained confirm the belief of many authorities that the beneficial effects of this form of therapy depend on the fever itself rather than on the way in which it is induced.

The obvious advantages of the physical methods of inducing artificial fever make them more desirable for the treatment of patients who do not require institutional care.

SUMMARY

The clinical and serologic results obtained in the treatment of eighty-seven patients with the various forms of neurosyphilis by means of drug therapy combined with artificial fever therapy are presented.

The fever was produced in this series by the blanket method.

The Wassermann reactions of the spinal fluid became negative or showed considerable improvement in 73.4 per cent of the patients of the entire series.

The colloidal gold curve became normal or improved in 77 per cent of the entire series.

The cell count was decreased to normal in 95 per cent of the cases in which abnormal counts had been obtained.

The protein and the globulin content of the spinal fluid were reduced to normal or improved in 74 per cent of the cases studied.

The Wassermann and the Kahn reaction of the blood did not respond as well as did those of the spinal fluid.

In two cases the spinal fluid relapsed and the reaction became positive, probably owing to inadequate follow-up drug therapy.

CONCLUSION

Artificial fever therapy is a valuable adjunct in the treatment of dementia paralytica, the tabetic form of dementia paralytica, tabes dorsalis, asymptomatic neurosyphilis and meningovascular syphilis.

ABSTRACT OF DISCUSSION

DR. H. N. COLE, Cleveland: I have been much interested in the results Dr. Epstein has achieved with this method of therapy and think he is to be congratulated on devising a simple scheme like this which obviates the necessities of high-priced apparatus and of carrying on a strain of malaria organisms in an institution, which is no small matter. It may even happen that the strain will die out, leaving a difficult situation when the next patient comes along. Apparently Dr. Epstein has obtained excellent results with this method. It will be interesting to follow his work, to observe its results in other clinics and to see how they differ from those of fever therapy and of other methods of inducing artificial heat. I have been much impressed with malaria therapy. It seems to me that there is something at work besides the fever, but I stand ready to be convinced.

DR. PAUL A. O'LEARY, Rochester, Minn.: I feel as Dr. Cole does, that Dr. Epstein should be congratulated for having devised a simple, inexpensive and economical apparatus which is apparently producing results similar to those obtained with the more expensive types of apparatus for producing fever.

In a study of the results of treatment of neurosyphilis the results following the use of the combination of fever therapy and medication with tryparsamide have been outstanding. The clinical and serologic results far surpass those of any other combination of therapeutic agents used in the treatment of neurosyphilis. That tryparsamide is the outstanding chemotherapeutic agent for the treatment of neurosyphilis is now well established. The point has not yet been reached at which it can be said that the fever per se is the factor which produces the favorable results of fever therapy, although it is feasible to assume that the fever produced may provoke the immunologic changes which in turn produce the satisfactory clinical and serologic results that follow fever therapy. Bessemans, of Brussels, who has been studying the effects of fever in laboratory animals for the past ten years, believes that the thermal death point of Spirochaeta pallida in the animal is not less than 112 F. Accordingly, I do not believe it possible to accept the idea with which the fever therapeutists started several years ago, namely, that S. pallida is "cooked" by the fever produced. The type of unit used to produce the fever is immaterial, as equally good results are obtained from all of them when used in conjunction with chemotherapy in the treatment of neurosyphilis.

DR. HOWARD MORROW, San Francisco: I think there is no question that fever therapy has come to stay. I have been deeply interested in the apparatus Dr. Epstein has made on the coast and which he has more or less perfected. My associates and I have used several kinds of cabinets, and all have been expensive. Recently we were invited to inspect the Kettering machine in Ohio, and on Monday we went there and looked at the outfit. I think the same results can be obtained with Dr. Epstein's apparatus that the Kettering people can get with their elaborate outfit. It takes a great deal of room for one of the Kettering cabinets. One of them occupies the space of an ordinary treatment room and requires the attention of one nurse for eight or nine hours, while the patient is in the cabinet. With Dr. Epstein's method one nurse can care for four patients.

which is a great saving. Four patients can be put in an ordinary treatment room. The patients are ambulatory. They are admitted early in the morning, put in the so-called blanket pack and kept there for five hours during the height of a fever. It takes about one hour for them to be sponged off. They are kept one night and in the morning go home. It is important that the nurse be well trained in the care of these patients and that the physician carefully select the patients for the treatment. To use heat indiscriminately is sometimes dangerous.

One thing I learned about on my visit to the Kettering headquarters in Dayton is the recording thermometer. Dr. Epstein used an ordinary thermometer at the rectum at first, but it was difficult to get at. Later the axillary temperature was used and this has proved satisfactory, although some physicians claim it is not accurate. At the Miami Valley Hospital, Dayton, are a number of recording thermometers which are of great value. One is placed in the rectum and kept there during the entire time of the fever, and from it one can read the temperature accurately from the outside. The rectum need not be touched during the entire time of treatment. The only objection is that these thermometers cost $200; but from my limited observation while in Dayton, I think they are worth it.

Dr. Earl D. Osborne, Buffalo: I wish to ask a few questions. First, is an attempt made to raise the temperature above 104 F., and if so, how high? Second, when were the examinations of the spinal fluid which were referred to in the paper made? I am sure that the results at the three, four and five year periods are much more favorable than those at the end of one year. Third, how much of the face and head is covered during the treatment? Is an attempt made to maintain the temperature of that part of the body, and is it necessary that the patient keep his eyes closed during the treatment?

I entirely agree with Drs. Cole and O'Leary that so far malaria is the best method of fever therapy. I have secured some excellent results from malaria therapy when the temperature did not exceed 101 or 101.5 F. In order to secure results with the fever box, it is always necessary to secure a temperature of over 104 F. Dermatologists are still in ignorance of the therapeutic mechanism of malaria therapy in syphilis.

Dr. John H. Stokes, Philadelphia: Methods of fever therapy which permit the patient to be ambulatory the larger part of the time are definitely needed. When tryparsamide is to be employed as a chemotherapeutic agent, attention should be given to the practice of Dr. W. F. Lorenz, of the University of Wisconsin, one of the pioneers in this field, who has recommended and is giving doses of as high as, or in some cases higher than, 5 Gm. of the drug weekly. The results of chemotherapy combined with the induction of fever by physical methods should be closely compared with those of inducing fever by malaria, for in my experience the single malarial course stands today as the most effective unit form of treatment for neurosyphilis. The serologic and clinical improvement of these patients as long as two or three years after one bout of treatment is remarkable. So far as I have observed, nothing in the field of physical therapy with fever duplicates this prolonged effect. Perhaps chemotherapy combined with fever therapy will show effects equal to those of the malarial course.

All users of pyrexial therapy need to maintain constant vigilance in the matter of mortality. A long series of good results without complications may precede an unaccountable death. Relaxation of vigilance, inadequate weighing of contraindications and the disposition to take a chance because one has got away with it before are the things that keep up the mortality statistics. It is interesting to observe the increased tolerance of heat exhibited by patients who have a small

area of skin—for example, the face, the hand or the foot—exposed to cool air. This has been observed in fever therapy obtained by the hot bath and was, I believe, noted by Bazett in some of his studies of cutaneous temperature.

Dr. Dudley C. Smith, Charlottesville, Va.: This paper of Dr. Epstein's should be given wide publicity and published in a general journal rather than in a publication for specialists. Simplification of medicine from the standpoint either of diagnosis or of therapy is worth while. The methods described certainly simplify the technic of fever therapy.

There are contraindications and definite hazards in the use of inoculation malaria. The many types of apparatus recommended during the last several years for producing artificial fever are expensive and require expert technical assistance. Most of them may produce various types of injury during their use.

It should be remembered that patients with neurosyphilis have, in addition, a generalized infection. This is an indication for general routine antisyphilitic therapy which cannot be given during the period of their malaria.

The method described in this paper is not only simple but effective and carries little risk either of immediate injury or of later untoward reactions. The automatically regulated tub bath in my experience has been just as effective in producing fever as the blanket method. Improvements in the technic and management of these methods of fever therapy which will come with more widespread use will probably result in their replacing other methods of fever therapy.

The preceding statements minimize the opinion of some that there may be a specific effect of the malaria itself, in addition to the effect of the temperature.

Dr. Norman N. Epstein, San Francisco: I wish to thank the discussers for their instructive remarks. It was not my intention to compare this form of fever therapy with the biologic methods of producing fever. I wish to call to your attention the fact that Schamberg showed that he could sterilize a syphilitic rabbit by means of hot water baths. Warren showed that he could cause spirochetes to become avirulent by heating them to 105 or 106 F. in a test tube. Bessemans has investigated the entire subject of heat therapy from an experimental standpoint, and he found that heat alone has a decided effect on S. pallida. I agree that heat is only one of the factors in this form of therapy. Heat alone has caused the disappearance of S. pallida from human chancres.

My results with malaria therapy have been excellent, but, as Dr. Stokes said, there has been need for treating ambulatory patients in some way that would not interfere with their carrying on their occupations. Treated in this way the patient maintains his position in the community, and drug therapy can be given simultaneously with the heat therapy.

DECIDUOUS SKIN

PAUL E. BECHET, M.D.
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Deciduous skin can be defined best as continuous, periodic or seasonal shedding or peeling of the epidermal layer of the skin of more or less generalized distribution.

A perusal of the literature of the past thirty years throws little light on this interesting subject, and much of the information elicited is sparse, confusing and contradictory. For example, Stelwagon [1] described deciduous skin under the general heading of erythema scarlatiniforme and expressed the belief that it is related to that disease. Sutton [2] stated that keratolysis exfoliativa of the palms and soles is synonymous with deciduous skin. MacKee and Lewis,[3] on the other hand, expressed the opinion that keratolysis exfoliativa is a clinical entity, probably a dermatophytid. Frank and Sandford's [4] celebrated case of shedding skin, observed by Hyde [5] and reported later by Sligh,[6] presented the classic features of erythema scarlatiniforme, namely, rapid rise of temperature, lassitude, weakness, muscular tremors, nausea and vomiting for several hours and generalized acute redness of the skin for thirty-six hours or longer, with separation of large sheets of it on the sixth day and of complete casts of the hands and feet by the seventeenth day. Similar cases have been reported by Stelwagon,[7] Stone [8] and others. In most of these cases there were characteristic symptoms

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Read at the Sixtieth Annual Meeting of the American Dermatological Association, Inc., Cresco, Pa., June 5, 1937.

1. Stelwagon, Henry W.: A Treatise on Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1921, p. 137.

2. Sutton, Richard L.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1926, p. 154.

3. MacKee, George M., and Lewis, George M.: Keratolysis Exfoliativa and the Mosaic Fungus, Arch. Dermat. & Syph. **23**:445 (March) 1931.

4. Frank, J., and Sandford, W. C.: A Remarkable Case of Skin Disease, Am. J. M. Sc. **102**:164, 1891.

5. Hyde, James Nevins: A Practical Treatise on Diseases of the Skin, Philadelphia, Lea & Febiger, 1909, p. 141.

6. Sligh, J.: Unique Case of Annual Shedding of Skin, Internat. M. Mag. **2**:463, 1893.

7. Stelwagon, Henry W.: Diseases of the Skin, ed. 5, Philadelphia, W. B. Saunders Company, 1907, p. 143.

8. Stone, R. M.: Keratolysis or "Skin Shedding," J. A. M. A. **35**:557 (Sept. 1) 1900.

of scarlatiniform erythema rather than a shedding skin without subjective symptoms or visible abnormality other than the peeling epidermis.

Keratosis exfoliativa is not uncommon. It is usually limited to the hands but occasionally involves the feet. The characteristic lesions are white macules, varying in diameter from 0.125 to 0.5 mm., the so-called empty vesicles or air bubbles. Within a few hours or several days the lesions exfoliate in the center, leaving collarets of loose epithelium as thin as cigaret paper. There is no inflammatory reaction, but occasionally true vesicles occur in the contiguous area. This dermatosis is occasionally placed in the category of shedding skin, but from the evidence it apparently does not belong there. It was first described in 1903 by Carayon,[9] of Dubreuilh's clinic at Bordeaux, France, under the title "Desquamation estivale en aires des mains."

In 1919 Wende [10] reported two cases under the title "Keratolysis Exfoliativa." Lane [11] stated:

> There is so little difference in the description by Carayon and by Wende that it seems probable that keratolysis-exfoliativa and desquamation estivale en aires des mains are identical.

MacKee and Lewis, after an extensive investigation of the literature and a careful study of three cases, stated that there is a common association of keratolysis exfoliativa with the vesicular or dyshidrotic type of dermatomycosis and that the former disease is probably a dermatophytid. In the discussion of MacKee and Lewis' paper Clark W. Finnerud made the following statement:

> We have come to believe, therefore, that a clinical picture similar or identical to keratolysis exfoliativa may be produced by the local action of demonstrable fungi, and, furthermore, that such a picture may result from the absorption of toxins from a distant fungus or bacterial focus, for in several cases we have noted classic keratolysis exfoliativa of the palms in association with an acute vesicular exacerbation of ringworm of the feet.

Arthur M. Greenwood in 1921 cultivated Microsporon lanosum in one case of keratolysis exfoliativa. In the discussion of MacKee and Lewis' paper Earl D. Osborne stated:

> During the past few months, we have made a study of a few cases diagnosed several years ago by Dr. Wende as keratolysis exfoliativa in patients who afterward came to the office with what we took to be ringworm of the palms. We have studied these cases and found a mycelial organism.

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9. Carayon, A.: Desquamation estivale en aires des mains, Ann. de dermat. et syph. **4**:283, 1903.

10. Wende, Grover W.: Keratolysis Exfoliativa, J. Cutan. Dis. **37**:174, 1919.

11. Lane, John E.: Some Observations on Keratolysis Exfoliativa, J. Cutan. Dis. **37**:223, 1919.

In view of this evidence, it would therefore seem to me more proper to place keratolysis exfoliativa in the group of dermatophytosis or dermatophytid and not to consider it as a simple shedding of the skin.

True examples of deciduous skin are extremely rare. Since 1911 only one case has been presented before a dermatologic society in America, at a meeting of the New York Dermatological Society on Oct. 26, 1920. The patient was exhibited by Fox.[12] The patient was a woman 28 years of age, and during her entire life she had suffered from periodic peeling of the skin in flakes similar to those of scarlet fever. The desquamation affected the entire body and was never associated with redness or any subjective symptoms. No one else in her family had ever had a similar condition. Her health was excellent. Examination showed a flaky desquamation on the trunk. There was no evidence of ichthyosis, her skin in general being remarkably soft and smooth. The hair and nails showed nothing abnormal. I have observed a similar case, a report of which follows:

REPORT OF A CASE

A man aged 22, born in the United States, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Sept. 5, 1936, for the relief of a desquamation which had been present since birth. For as long as he could remember the peeling began in May, lasted throughout the summer and subsided by October. During the winter he was entirely free. The patient was extremely intelligent. He stated that his sister suffered from a similar periodic shedding of the skin, also present since birth. No other member of the family was affected, and his father and mother were not related. The patient stated that his desquamative phenomenon was greatly aggravated by the slightest friction. His general health had always been excellent, and he said that there were no subjective symptoms.

Inspection revealed a well nourished healthy man of splendid physique, with areas of superficial desquamation on the upper part of the trunk and arms. A peculiar and constant phenomenon was the exfoliation produced by friction almost anywhere on his body but especially on the upper part of the trunk and the arms. By rubbing an apparently normal area of skin with the finger, the epidermal layer could be removed, and a slightly glazed and reddened surface remained; the redness subsided in an hour or so, leaving only the exfoliated area. The texture of the skin was smooth and soft, without the slightest suggestion of ichthyosis. The patient's teeth, hair and nails were normal. A complete physical examination revealed nothing abnormal. A blood count, a urinalysis and the Wassermann and the Kahn test showed no abnormality.

In a histologic study of tissue Dr. D. L. Satenstein noted little that helped to explain the clinical picture. There was a poorly developed, laminated horny layer. The rest of the skin presented no changes.

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12. Fox, Howard: Skin Shedding (Keratolysis Exfoliativa Congenita), Arch. Dermat. & Syph. **3**:202 (Feb.) 1921.

CONCLUSIONS

1. The evidence in the recent literature and that gathered by personal observation make it seem more plausible to place keratolysis exfoliativa in the group of dermatophytosis or dermatophytid.

2. In a large majority of cases the condition described as deciduous skin presents the classic symptoms of erythema scarlatiniforme and cannot be clinically differentiated from it. The condition in those cases, therefore, should be considered as a phase, typical or atypical, of that disease and not as deciduous skin.

3. Dr. Fox's case and mine are examples of an extremely rare clinical entity, probably hereditary, which is characterized by a more or less severe, simple peeling of the skin, without inflammatory changes or subjective symptoms. The term keratolysis exfoliativa congenita, hitherto used in describing this dermatosis, is misleading and can easily be confused with the term keratolysis exfoliativa of the hands, which designates an entirely different cutaneous disease. Until a better name is conceived, it might be best to call these rare manifestations of exfoliation congenital shedding of the skin.

ABSTRACT OF DISCUSSION

Dr. Howard Fox, New York: I am surprised to hear that shedding of the skin is so exceedingly rare. My patient, whom Dr. Bechet has mentioned, showed no clinical evidence of inflammatory changes in the skin, and she assured me that there had never been any redness which might have suggested scarlatiniform erythema. Her general health had always been excellent.

Dr. James H. Mitchell, Chicago: In a discussion of the differential diagnosis of scaling palms attention should be called to one type of exfoliation of the palms, which results from the ingestion of quinine tablets for colds. I have seen four attacks in one patient. There is sometimes little eruption on the body, but the cold tablets cause exfoliation of the palms.

Dr. H. H. Hazen, Washington, D. C.: I have observed one case of deciduous skin in a physician. He had had the trouble from early childhood. The trouble was traced to soap containing coconut oil. When this was eliminated he recovered. Later he used a coconut oil shampoo, and an eruption promptly developed over the face and the chin.

Dr. Samuel M. Peck, New York: It must be remembered in the differential diagnosis of other scaling eruptions of the palms, that histologically even scaling so-called squamous dermatophytid is vesicular eczema. I have reported a scarlatiniform eruption which proved to be trichophytid.

Dr. Fred D. Weidman, Philadelphia: It might be instructive to analyze these sheddings of skin according to the time of the year at which they occur in order to determine whether the condition could be a phylogenetic phenomenon. Certain animals, such as snakes, shed their skins at certain times of the year, and others shed their hair. Von Louenhouck, who was a careful observer, reported a seasonal shedding of his own hair.

DR. ERICH HOFFMANN, Bonn, Germany (by invitation): In a paper on the importance of comparative and general physiopathologic study of the skin I have stated that exfoliatio chronica palmarum is a superficial intermittent disease, which may be considered similar to moulting in birds.

DR. W. H. GUY, Pittsburgh: I am inclined to suggest that this condition is due to an endocrine disturbance. The one condition that resembles it histologically is dermatitis exfoliativa neonatorum, which is not a dermatitis but a congestive disease characterized by a separation of the corneous layer like that demonstrated in Dr. Bechet's case. In two cases of Ritter's disease in which autopsy was performed there was almost complete displacement of adrenal tissue by hemorrhagic cysts. The fact that deciduous skin occurs seasonally suggests the advisability of investigating all cases for a possible endocrine imbalance.

DR. PAUL E. BECHET, New York: The paper elicited more discussion than I had anticipated, and I am grateful for it. The patient sheds his skin between May and October, and the fact that this has been going on since birth naturally eliminates soap as an etiologic factor.

In answer to Dr. Hoffmann's discussion, I wish to state that the patient has never had any palmar exfoliation. My chief reason for the presentation was that the dermatosis is apparently extremely rare, at least in this country, for in the past twenty-six years only one case has appeared in the American literature. I hoped through the evidence submitted possibly to clarify the classification of a definite dermatologic entity, which hitherto has apparently been confused with other manifestations of exfoliating skin entirely unrelated to it.

SYPHILIZATION

AN EPISODE IN THE EVOLUTION OF SYPHILOLOGY

ARTHUR W. STILLIANS, M.D.
CHICAGO

Before 1843 Ricord had demonstrated by a long series of inoculation experiments that gonorrhea is a disease distinct from the venereal ulcer, thus producing the first rift in the fog of confusion created by Hunter over a half-century earlier. In a more limited sense, however, Ricord and his school were still unicists; they believed that all venereal ulcers were primary lesions of syphilis. In that day chancroid was much more common than it is today and apparently more common than the indurated sore. It was thought that if the soft venereal ulcer were neglected and if the patient were in a certain bodily condition "constitutional syphilis" might develop. The hard chancre was a little understood, rather puzzling phenomenon, considered merely an indication of a transitional stage in the development of the disease. Some called it the "pseudo-chancre." Ricord recognized that there was a difference between the soft venereal ulcer and constitutional syphilis, for he did not treat the soft ulcer with mercury, having noticed that that drug seemed to have an unfavorable effect. Instead, he cauterized it with a mixture of lime and potassium hydroxide, and believed that early cauterization prevented the development of constitutional syphilis.

Ricord was accustomed to using auto-inoculation to prove the syphilitic character of the venereal ulcer. If a pustule developed promptly at the site of inoculation the ulcer was considered syphilitic and cauterized. If a pustule did not develop, the ulcer was considered a simple one, requiring only mild treatment. It was therefore a daily experience of the pupils and interns working with Ricord to see auto-inoculation practiced.

During a lecture in 1843 Ricord stated that animals cannot be infected with syphilis. This statement aroused opposition in the mind of one of his interns, Joseph-Alexandre Auzias-Turenne, a recent graduate, somewhat overstocked with self-confidence, who determined to try it. Other diseases were transmissible by inoculation of animals, he thought; why not syphilis? Assisted by his friend Étienne Geoffroy-Saint-Hilaire, author of "Philosophie anatomique," he procured a monkey, the

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animal most resembling man and most likely, he thought, to be susceptible to his diseases, and inoculated it with pus from a venereal ulcer. The monkey promptly licked the wound, and the inoculation failed to produce any result. Auzias-Turenne then obtained a monkey that had been paralyzed in some way and inoculated it on the paralyzed side. Success attended this experiment. Later he learned to choose the proper site and to inoculate more superficially and thus could get a large percentage of successful results. Besides monkeys he inoculated rats, cats, dogs, foxes, rabbits and even a goat. In some of these animals he described the development of papules, moist lesions, osseous lesions and other manifestations that he thought indicative of syphilis.

When he practiced auto-inoculation on these animals, he was struck by the fact that successive inoculations resulted in successively smaller ulcers until at last no pustule resulted. A fresh inoculation from a human source would succeed, but after a series of auto-inoculations this infection too failed to produce pus. Finally the skin of the animal became so resistant that inoculation of venereal pus from any source was unavailing. This Auzias-Turenne considered immunity to syphilis, comparable to immunity to smallpox resulting from vaccination. In October 1844 he announced to the Academy of Science in Paris his success in inoculating animals with syphilis and demonstrated his experimental animals to the Academy of Medicine and the Society of Surgery.

Applied to human beings with resistant venereal ulcers, the method of repeated auto-inoculation and hetero-inoculation resulted in cure of the old ulcers and aroused in Auzias-Turenne such enthusiasm that he proposed the use of "syphilization," as he called it, not only for treatment but for producing immunity to syphilis and thus eradicating the disease as smallpox had been practically eradicated by vaccination. All prostitutes, soldiers, sailors, persons who worked in prisons, public baths or factories and doctors he would protect from syphilis by this method.

Although reasonable, had the initial premise been correct, this proposal aroused intense opposition and a long controversy with Ricord, which often became acrimonious. One of Ricord's favorite taunts was to ask why, if syphilization was so excellent a measure, the originator of it did not practice it on himself. Auzias-Turenne replied that to do this would expose him to derision and his character to calumny. In his will, however, Auzias-Turenne stated that he was the first human being to undergo syphilization, and the scars found on his chest at the autopsy bore out the statement. So great was the influence of Ricord and his school that Auzias-Turenne could not get the opportunity to demonstrate his method of treatment on patients in the Paris hospitals, and years later even the influence of Prince Napoleon was insufficient to gain for him permission to use a few beds in the Prison St. Lazarre to demonstrate the method on volunteers among the women patients.

Robert de Welz, a healthy young man who had never had syphilis, allowed himself to be inoculated with pus from the experimental ulcers produced on monkeys and cats. The ulcers resulting from these inoculations were pronounced by Ricord identical with human venereal ulcers but "still not syphilis." He advised cauterization to prevent further development.

Although refused recognition in France, the ideas of Auzias-Turenne were received with more hospitality in Italy, where Sperino, of Turin, became the chief disciple and practiced syphilization extensively. The Scandinavians developed syphilization conservatively and found it a successful means of treating syphilis. Wilhelm Boeck, of Christiania, Norway, reported 100 cases of constitutional syphilis in which this method had been used and among which there had been only three relapses. He considered that there were less danger, more constant success and less tendency to relapse than with treatment by mercury and iodides.

Auzias-Turenne arrived at the idea of syphilization through experimentation with animals and in this respect was a pioneer; but he was far from being the first to use auto-inoculation and hetero-inoculation in the treatment of venereal ulcer. In the early nineteenth century many Italian and English practitioners and quacks had practiced inoculation for the cure of obstinate venereal ulcer. Baron Percy, a military surgeon, used dried pus of venereal ulcers to treat obstinate chancroid and with this method succeeded where all others had failed. This was mentioned in a report by Fabre to the Academy of Surgery in 1783. Carmichael,[1] of Dublin, Ireland, tried auto-inoculation before 1814 but did not develop it. Fricke, of Hamburg, Germany, quoted by Graves [2] in 1838, said:

> If a person affected with chancres were inoculated with the matter of that chancre on a fresh spot and from this on a third and so on it will be found that this process can be repeated only a few times with success. The individual becomes, as it were, habituated to the virus and less capable of its influence.

This previous work was not known to Auzias-Turenne until long after he had developed syphilization.

It was inevitable that Auzias-Turenne and his more enthusiastic pupils should come to grief on the proposal to use syphilization to immunize healthy persons against syphilis. Lindeman, a German disciple, inoculated himself twelve times in 1850 and 1851 but produced only soft ulcers. The thirteenth attempt, however, produced a hard

1. Carmichael, J. R.: An Essay on the Venereal Diseases, ed. 1, Philadelphia, Thomas Dobson & Sons, 1817, p. 249.

2. Graves: Clinical Lectures on Medicine, London Med. Gaz. **1**:697, 1838-1839.

chancre on the forearm, which was followed in three months by roseola, mucous patches and syphilitic papules. Treatment by syphilization was not successful, seeming to harm rather than to help, and he rapidly declined and died. In discussing this case, Ricord [3] wrote in 1851:

> In the mean while, the conclusion which results from the analysis which I have made of the published observations made at Paris and Italy, is, that the pus which comes from non-indurated chancres has always been inoculated to produce analogous accidents; and that in the only instance in which the pus from a primitive accident which had produced a constitutional syphilis was used at Paris to inoculate a patient who was healthy, the individual was affected with an indurated chancre and a general poisoning. Were it always thus, as I have already stated, it would be necessary to come to this conclusion; that differences may exist in the disease which do not depend upon the conditions of the affected individual alone, but also upon differences in the causes of the disease.

Thus began his doubt of unicism and trend toward dualism, but years of observation were necessary to convince him completely.

Carmichael,[1] of Dublin, Ireland, was an early doubter of unicism who attempted in 1814 to classify the venereal diseases but did so with no clarity. Morgan [4] in 1837 supported Carmichael's views. In 1852 Bassereau,[5] a pupil of Ricord, brought out a convincing argument against unicism based on clinical observation and confrontation. He distinguished the "chancre with suppurating bubo" from the "chancre which precedes constitutional infection." Valuable experimental evidence on this subject resulted from the attempt of Danielssen,[6] of Bergen, Norway, to use syphilization in the treatment of leprosy. Convinced, after long observation, of its efficacy in the treatment of syphilis, he thought to try its effect on leprosy. He first inoculated lepers with the pus of soft venereal ulcers; but instead of reinoculating, as the syphilizers did, he waited for the appearance of secondary syphilids, to see whether secondary syphilis would have an effect on leprosy. No secondary symptoms appeared, although he waited for months. He then used the regular method of syphilization, with good effect in syphilis but without benefit in leprosy. After a series of nearly four hundred inoculations of chancroidal pus, without benefit, in one of these lepers, the secretion of a hard chancre was used by mistake. A month later a hard chancre appeared at the site of inoculation and was followed in due

3. Ricord, P.: Letters on Syphilis, translated by W. P. Lattimore, Philadelphia, Blanchard & Lea, 1854, p. 248.

4. Morgan, G. T.: Observations on the Question, Whether the Symptoms Indicative of the Presence of Lues Venerea Depend on One or Several Distinct Poisons, Edinburgh M. & S. J. **47**:166, 1837.

5. Bassereau, P. I. A. L.: Traites des affections de la peau, Paris, J. B. Ballière, 1852, p. 182.

6. Danielssen, D. C.: Syphilization as Employed in Syphilis and Leprosy. Brit. & For. Med.-Chir. Rev. **23**:118, 1859.

time by roseola, mucous patches and syphilitic papules. Thus, by one mistaken procedure, the failure of syphilization to protect against syphilis and the fallacy of the unicistic theory were demonstrated.

Although it is now apparent how greatly Auzias-Turenne was misled in his interpretation of the experiments on animals, it is just as clear that his false conclusions were due partly to the custom of reasoning by analogy, a practice of the greatest men of his time, but more to the lack of knowledge concerning syphilis and chancroid and to the false theory of unicism. One cannot doubt the sincerity of the founder of this peculiar method of treatment or the truth of the statement of his followers and others that the inoculations were beneficial in secondary and tertiary syphilis of the skin. Only of late years has it become apparent how beneficial therapy with foreign proteins can be in resistant syphilis, and to my mind it is not stretching the imagination too far to consider syphilization a kind of therapy with a foreign protein.

Cole and Levin [7] have recently shown the beneficial results of a vaccine made from chancroidal pus in the treatment of chancroid. Auzias-Turenne and his followers used the living virus with similar results.

In spite of the fallacy connected with syphilization, the practice of it resulted in clinical evidence in favor of the dualistic theory, helped to destroy the theory on which syphilization was founded and added to the knowledge of syphilis. Auzias-Turenne's technic of animal inoculation was excellent. Proksch [8] said of him: "It is certain that before and also after Auzias-Turenne nobody devoted more time, attention and care to animal experimentation upon syphilis."

In 1873 Bumstead,[9] of New York, a noted authority on venereal disease, wrote an article describing the visit of Wilhelm Boeck, of Christiania, Norway, to New York. During his stay in this country Professor Boeck demonstrated on one of Bumstead's patients that by sufficient irritation the secretion of a hard chancre can be made to produce an ulcer on the skin of a syphilitic patient. To Bumstead this seemed difficult to explain in accordance with the dualistic theory. Hyde,[10] of Chicago, answered with the explanation that by any irritation it is possible sometimes to produce secondary lesions on syphilitic skin even in advance of the normal secondary stage. In addition, Hyde took

7. Cole, H. N., and Levin, E. A.: The Intradermal Reaction with Chancroidal Bubo Pus, J. A. M. A. **105**:2043 (Dec. 21) 1935.

8. Proksch, J. K.: Geschichte den venerischen Krankheiten, Bonn, P. Hanstein, 1895, pt. 2, p. 771.

9. Bumstead, F. J.: On the Present State of the Question of the Unity or Duality of Syphilis, Am. J. M. Sc. **65**:321, 1873.

10. Hyde, J. N.: On the Unity or Duality of Syphilis, Chicago M. J. **30**:530, 1873.

the opportunity to answer an article in the *Chicago Medical Examiner* in which Andrews,[11] evidently exasperated by the lengthy, often vague and even contradictory arguments of the syphilographers of that day, broke out with:

> The fluctuations of this remarkable controversy are adapted to arouse indignation in a thinking mind. What is the use of science in the hands of men who contrive not how to bring out solid and permanent truth; but only some startling conclusions upon which to base a reputation? Who are these pseudo great men to whom we have given the highest honors of science for forty years for telling us first, that the syphilitic virus is single, then that it is undoubtedly double, then again that it is single and finally, that they don't know which it is? Would any blockhead have done worse by simple guess work? There is only one remedy for this foolery, and that is to leave off honoring men for half made discoveries and to scourge with the lash of criticism and contempt all efforts to place crude and ill-sustained opinions in the rank of ascertained truths.

This was an invitation to flay a critic of Ricord and a member of a rival faculty, and Hyde rose to the occasion. His reply seems a fitting close to this small excursion among the problems of a century ago:

> Without attempting to criticize the rhetoric or spirit of this contemptuous "lash" it may be profitable to remind him that "solid and permanent truth" is most often attained by a process of "half made discoveries." Rarely is it allotted to one man to subtract all the golden ore from its hidden veins. Piece by piece, with much alloy, through arduous labor and by the aid of fellow workmen, is it brought to the crucible. Columbus never saw the mainland of this continent; but it is inscribed upon his tombstone that "he gave a new world to Castile." Bichat, Hunter, Paget and Virchow have been justly honored, though they gave many half truths to the world and often less than that. And were the doctrines of dualism to be tomorrow disproved, they who have toiled and studied and written to set them forth would be chiefly honored for their contribution to the final result.

ABSTRACT OF DISCUSSION

DR. CHARLES C. DENNIE, Kansas City, Mo.: This is a historical paper of great interest. One of the first experiments carried out to ascertain the cause of syphilis, even before the disease was named syphilis, was made by one Leonardo Fioravanti in Naples, Italy, at the time that King Charles VIII of France was attempting to capture that city. When the French came across the mountains they could not take their food with them, and they soon ran short of provisions, but this Fioravanti, who was a Neopolitan physician, was interested in the fact that, while the French brought no food at all from the outside, they were supplied with meat. He investigated and found that their meat was coming from the bodies of those who had died of syphilis. In his report he said, "I became suspicious that cannibalism is the cause of syphilis, so I took a sow into my own bedroom and fed it on nothing but pork. Its hair fell out and it developed sores on its body. Not satisfied, I took a dog and fed it in the same way, and its hair fell out. Therefore, I have come to the conclusion that cannibalism is the cause of syphilis."

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11. Andrews, E.: The Unity or Duality of the Syphilitic Virus, Chicago M. Exam. **12**:378, 1873.

When Columbus first came to the "New Islands," the natives were cannibals. Fioravanti thought that the cannibalism spontaneously produced syphilis in the natives. Thus, Columbus and his men, coming in contact with them, were infected and carried the plague back to Spain, giving reason to Fioravanti's experiments.

DR. PAUL E. BECHET, New York: Dr. Stillians' paper is a valuable contribution to the history of syphilis. If there are members who are inclined to smile, perhaps even superciliously, at the vagaries of the leaders of the past, I should like to remind them of the association's discussion on Wednesday of the epidemiology of leprosy, contemplation of which makes an excellent antidote for ego.

DR. ARTHUR W. STILLIANS, Chicago: Auzias-Turenne is to be credited with the fact that from 1851 on he was an ardent advocate of the theory of infectivity of secondary lesions of syphilis, which was not Ricord's belief. In 1855 he lectured to the American Medical Society of Paris; the two Boecks of Christiania, Norway, were present as guests. One of the chief arguments advanced was the infectiousness of certain secondary syphilids.

Listening to the discussion on leprosy the other night, I was reminded that Hansen thought the discovery of soap was one of the great factors in clearing up leprosy in Europe, and it occurred to me that this might have something to do with the present scarcity of chancroids. Monuments are erected to unknown heroes. Why not one to the unknown discoverer of soap?

THE SUPERFICIAL INTRA-ORAL USE OF ROENTGEN RAYS

A REPORT OF THE USE OF THE CHAOUL TUBE

LESTER HOLLANDER, M.D.
AND
JOSEPH M. SHELTON, M.D.
PITTSBURGH

In 1934 one of us (L. H.) with A. Fisher[1] published a short communication on the use of direct roentgen irradiation of intra-oral tumors with a home-made, somewhat clumsy apparatus designed by him and put in use in 1932 independently and without knowledge of any similar work elsewhere. The chief disadvantage of this apparatus was the length of time required to obtain the desired dose.

Later we became acquainted with a specially designed roentgen ray unit which serves the purpose of intracavitary irradiation much better than the aforementioned apparatus and has for an additional purpose simulation with roentgen ray energy of the effects of radium. It is known as the Chaoul contact therapy unit. In September 1936 we installed such an apparatus and have been greatly impressed with its value. We feel confident that the present report is justified, because it calls attention to an efficient and powerful agent for the attack of intra-oral carcinoma and other recalcitrant lesions of the oral cavity.

DESCRIPTION OF APPARATUS

The source of high tension employed in the apparatus is a simple constant potential generator, using a Greinacher circuit, which has a maximum output of 60 kilovolts and 4 milliamperes. It is housed in a cabinet, the top of which contains the control switches and various meters for timing, voltage and milliamperage.[2]

The tube is "shock proof." The radiation emanates from the distal end of a grounded metal tube; the roentgen rays emerge through a target of nickel and a water-cooling jacket which surrounds the anode. Thus the roentgen rays are filtered through water and a thin nickel window. The amount of filtration is approximately that of 0.2 mm. of nickel.[3]

From the Pittsburgh Skin and Cancer Foundation.

1. Hollander, L., and Fisher, A.: Superficial Intra-Oral Application of Roentgen Rays, Arch. Dermat. & Syph. **30**:793-795 (Dec.) 1934.

2. Pendergrass, E. P.: Roentgen Therapy by the Method of Chaoul, Am. J. Roentgenol. **35**:101-105 (Jan.) 1936.

3. Morison, Woodburn; Hugo, D., and Mayneord, W. V.: A Preliminary Note on Low-Voltage X-Ray Therapy, Brit. M. J. **2**:783-784 (Oct. 26) 1935.

The distal end of the tube is designed so that variously shaped and variously sized metal applicators can be slipped over it; these applicators limit the field of irradiation and insure constancy of the focal distance (3 or 5 cm.).

The stand for the tube is ingeniously constructed so that any desired position can be obtained and maintained. (The applicator remains in position by pressure against the part to be irradiated.)

An ordinary dental chair is used for the patient, who sits with his head resting on the double-cushioned extension of the chair.

It was previously mentioned that the tube is water cooled. We have installed an ordinary self-filling tank on an upper floor as a reservoir for the water. This

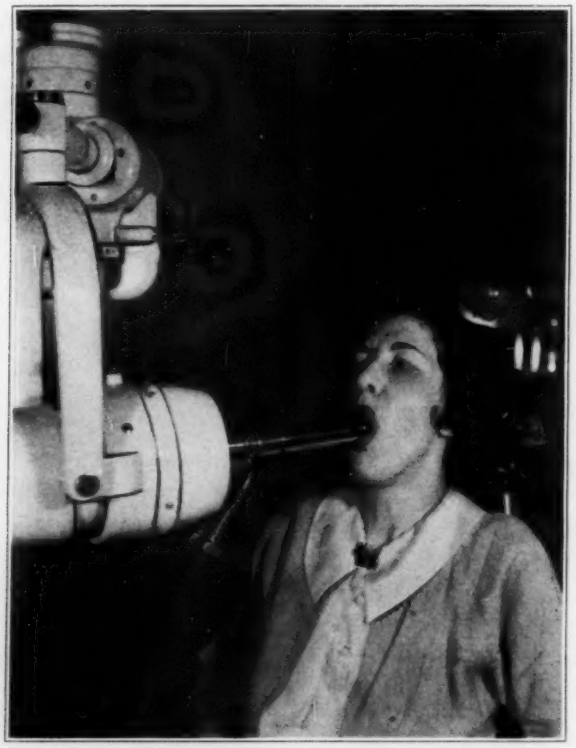

Fig. 1.—Chaoul tube in position for treatment.

insures an even pressure at all times, in contrast with the variable water pressure obtained from a direct connection with the city water supply.

Several safety devices are incorporated in this apparatus. On the work panel there is a timer which must be set when the machine is put in operation. This timer shuts off the current automatically if its signal (a buzzing sound) is not heeded by the operator. The current will not flow unless the water is circulating in sufficient volume.

SOME THEORETICAL CONSIDERATIONS

While in our original work we were attempting to reproduce within the mouth therapeutic effects obtained on the surface with massive

doses of roentgen rays, Chaoul's attempts were based on an entirely different principle.[4]

Contact irradiation was used because the apparent superiority of radium to roentgen therapy was due not to the actual quality of the rays but solely to the physical and technical method of application. This opinion was confirmed by physical measurements and other experiments by Holthusen, Braun, Hamann and others, whom Chaoul cited.

Thus Chaoul aimed at the production of roentgen irradiation which would resemble radium therapy in (1) geometric distribution, (2) time and (3) dosage.

In radium treatment the energy within the treated area declines quickly both below the surface and at the sides, thus permitting the administration of high destructive doses at the center of the diseased area without much harm to the surrounding healthy tissue. This is important as far as the subsequent healing process is concerned, since the viability of the adjacent tissue cells is preserved.

On the basis of these observations, Morison and his associates [3] and Pendergrass [2] brought out the following points with regard to the advantages of this new form of therapy: (1) The clinical effect of the same dose of roentgen irradiation is biologically the same for different wave lengths; (2) the energy absorbed per cubic centimeter of tissue and the interval between treatments are important factors; (3) healthy surrounding tissues should not be unnecessarily irradiated, so that their ability to repair the damage occasioned may not be interfered with; (4) the distribution of radiation in the tissues with short focal distances is similar to that obtained with surface applicators of radium and radium "bombs"; (5) as the initial financial outlay is small compared to that required for purchase of an equally effective amount of radium, and as the time of treatment is short, the apparatus makes treatment available for those who otherwise would not be able to get it; (6) Coutard based his treatment on the assumption that daily applications of small quantities of radiation tend to increase the tolerance of the skin and that the success of the method may depend on fractionating or protracting the dose; (7) the Chaoul method of contact therapy resembles the Coutard method of treatment in that a large total dose is built up by small daily treatment.

TECHNIC

In the ordinary case no special preparation is needed. The area to be irradiated is well exposed, and the applicator which fits it best is selected, placed on the tube and approximated to the lesion. It is fixed in position with slight pressure on the soft tissues of the mouth. The locks are then adjusted on the tube stand.

4. Chaoul, H.: The Treatment of Malignant Tumours by Concentrated Fractionated Short-Distance Irradiation, Strahlentherapie **53**:202-209, 1935.

If the lesion is tender it may be necessary to cocainize it with a 2 to 10 per cent solution by topical application. It is important to have the patient relax and remain quiet during treatment.

Our main objection to the apparatus is that it is difficult to approximate the applicator to the lesion accurately, since there is no light to guide one. Patience and a little experience are needed to get the best approximation.

DOSAGE

Chaoul and Morison use 400 roentgen doses daily per field for a maximum of from 6,000 to 9,000 r. We have been using from 540 to 550 r per field daily, treating as many fields as were necessary to cover the lesion. Our maximum dose varied from 10,000 to 40,000 r. The usual course consisted of twenty consecutive daily doses of 540 r.

Fig. 2.—Carcinoma of tongue, *A*, before treatment, March 20, 1937, and *B*, after reaction subsided, May 10, 1937.

REACTION

Mild erythema appears on the mucous membrane about the fifth day. As the treatments are continued, the severity of the erythema increases; the border becomes especially red, showing the outline of the applicator, and continues to become more pronounced until the end of the course; the center becomes covered with a yellowish necrotic film, which persists for from two to four weeks after the usual twentieth treatment has been given.

REPORT ON PATIENTS TREATED

Fourteen patients with carcinoma of the tongue were treated; among these were two with early and twelve with advanced involvement. All the latter presented palpable lymph nodes in the submental or the cervical region. Duration of the lesion ranged from three to twelve

months (in one instance three and a half years). The total dose varied from 10,000 to 30,000 r per field. In four instances the local lesion disappeared entirely; in six it improved markedly; in one it was unimproved, and in three the patient died.

Fourteen patients with carcinoma of the buccal mucous membrane were treated. Among these were one with early and thirteen with advanced conditions, four of the latter having palpable lymph nodes. Duration of the lesion ranged from three months to three years (in two instances ten years). The total dose varied from 10,000 to 30,000 r per field. In six instances the local lesion disappeared entirely; in five it was improved; in two it was unimproved, and in one the patient died.

There were five patients in the series with carcinoma of the pharyngeal wall and tonsils. Among these were two with early and three with advanced involvement, all the latter presenting palpable lymph

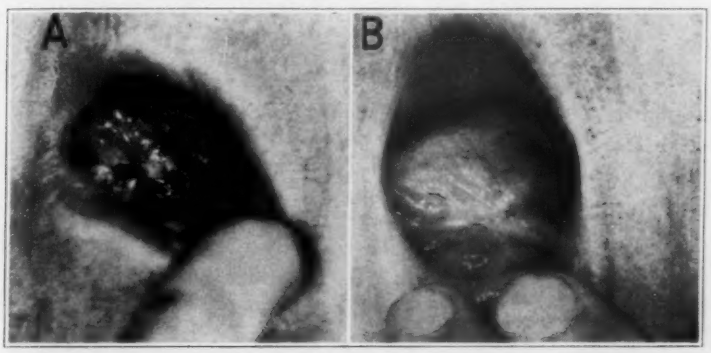

Fig. 3.—Carcinoma of tongue, *A*, before treatment, Feb. 23, 1937, and *B*, after reaction subsided, May 10, 1937.

nodes. Duration of the lesion ranged from two to six months. The total dose varied from 2,000 to 26,000 r per field. In all the patients the local lesions disappeared.

Three patients with carcinoma of the hard and soft palate were treated. In all the condition was advanced (of from two to thirteen months' duration), and there were palpable lymph nodes. The total dose ranged from 8,000 to 15,000 r. In all the patients the local lesion disappeared.

Two patients with carcinoma of the alveolar ridge were treated. In both the condition was in an early stage, without palpable lymph nodes, having existed for two and for ten months, respectively. Each received 10,000 r, and the local lesion disappeared in each instance.

Four patients with intra-oral sarcoma were treated. In one the condition was in an early and in three in an advanced stage. The duration

varied from three to eight months. The total dose ranged from 10,000 to 24,000 r per field. Two patients were improved; one was unimproved, and one died.

Four patients with intracavitary (but extra-oral) carcinoma were treated. In two the involvement was intranasal; in one, intravaginal,

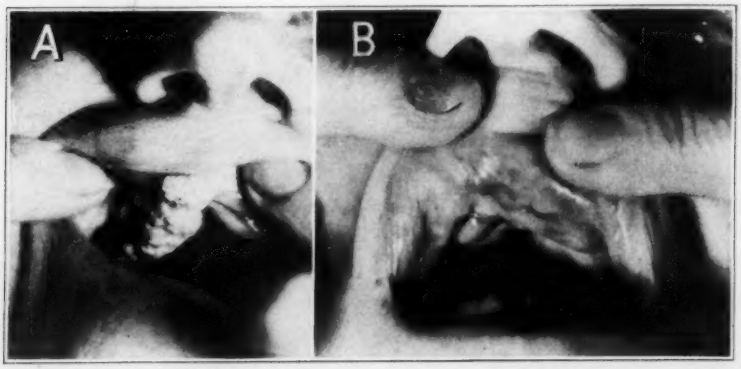

Fig. 4.—Carcinoma of alveolar ridge, hard palate and buccal mucosa, *A*, before treatment, Feb. 16, 1937, and *B*, after reaction subsided, May 17, 1937.

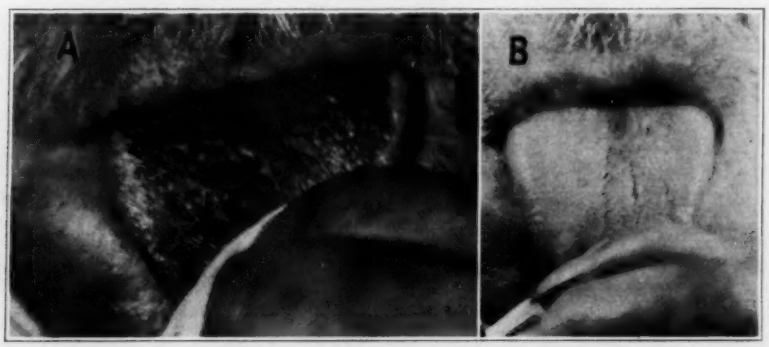

Fig. 5.—Lingua nigra, *A*, before treatment, Dec. 21, 1936, and *B*, after treatment, Feb. 23, 1937.

and in one, rectal. The total dose ranged from 6,000 to 18,000 r. Three patients were improved; one was unimproved.

Five patients with nonmalignant intra-oral lesions recalcitrant to other forms of therapy were treated. Three of these had extensive leukoplakia and two lingua nigra. The dose ranged from 2,000 to 5,000 r per field. The lesion disappeared in each instance.

SUMMARY AND CONCLUSIONS

Contact roentgen therapy for intra-oral carcinoma is discussed.

The apparatus, dosage and technic are described.

The advantages of this form of treatment are: the ease of treatment, the relatively low cost, the availability to a large number of patients, the surprisingly good results and the flexibility of the apparatus.

The disadvantage is the difficulty of visualizing the lesion to be treated.

ABSTRACT OF DISCUSSION

DR. F. M. JACOB, Pittsburgh: I had the opportunity of observing a number of Dr. Hollander's cases. One in particular, in which there was a large carcinoma of the buccal mucosa and the alveolar process, I was able to follow for a year or more after Dr. Hollander had finished his treatment and the tumor had disappeared. I can concur in Dr. Hollander's statements about the disappearance of these lesions. They disappear nicely in the majority of cases, and the scar is flexible comparable to scars resulting from other types of irradiation.

The reactions which occur strike me as somewhat similar to those following interstitial irradiation. I have had some experience with implantation of platinum-filtered seeds of radon, and the reactions which occur after the implantation of such seeds are comparable to the reactions which I saw in Dr. Hollander's cases. There are, of course, the advantages that the inflammatory reaction which follows the insertion of the seeds is eliminated and that a great number of patients may be treated economically, while treatment with the seeds is somewhat expensive.

The lack of trauma may be of importance. Dr. Hollander is of the school that think the disturbance of the tumor in the tumor bed is not a good thing. I am of the opinion that biopsy is of great importance.

The treatment of nonmalignant lesions was rather striking because dermatologists all know that treatment of leukoplakia and other lesions of the mouth is sometimes extremely difficult and with a radium pack or radium needles is not satisfactory.

As to the visualization, it was rather striking to me that even though at the time of irradiation these lesions could not be seen, within a few days the reaction began to occur and the lesion was so well outlined that the operator could easily see exactly where his radiation was hitting.

DR. ANTHONY C. CIPOLLARO, New York: I congratulate Dr. Hollander for bringing this technic to the attention of American dermatologists. I think he is the first dermatologist to report on this method of treating intra-oral carcinoma.

I should like to emphasize two points: first, that the form of radiation incorporated in the Chaoul technic is low voltage, moderately filtered radiation, and, second, that the results depend on the cauterizing effect of the roentgen rays applied.

A scar that follows treatment of a benign lesion with chemical or actual cautery is safer than one which follows treatment with radiation. A scar that results from irradiation, whether by radium or by roentgen rays, is a potentially dangerous lesion—far more dangerous than the patch of leukoplakia or the verruca which it replaced. Roentgen scars make favorable soil for the development of malignant growth. Therefore, in the treatment of benign lesions of the oral mucosa, the cauterizing effects of radium or roentgen rays should be avoided.

There are certain definite limitations in the application of this technic. In the first place it can be used only on small lesions, for only a small area can be treated at one time, an area no larger than that of the anode of the Chaoul tube. In the second place, the original cost of the apparatus is high. The complete installation costs in the neighborhood of $4,000. The comparatively few lesions which can be treated by this method and the original high cost of the equipment limit the use of the apparatus to institutions.

So far as I am able to judge from published works, the results obtained in treating intra-oral carcinoma by this method are no better than those obtained by the use of conventional therapy or radium therapy.

It must be borne in mind in the treatment of intra-oral carcinoma that the most important thing is the treatment of the lymphatic glands. A malignant growth in the mouth metastasizes quickly, rapidly and early. Cauterizing the local lesion by means of low voltage roentgen rays will cause disappearance of the tumor from the mouth. There still remains to be administered the most important part of the treatment—that to the lymphatic areas.

Dr. H. J. Templeton, Oakland, Calif.: The Chaoul tube emits rays which differ from those given off by customary superficial roentgen therapy tubes only in that they are of 60 kilovolt peak compared with from 90 to 100 for superficial roentgen therapy. I should like to ask Dr. Hollander if he thinks this difference in kilovoltage causes the rays to have different biologic actions.

The advantage of this tube would seem to be that the anode is close to its aperture or opening, so that the rays can be applied directly to intra-oral lesions. Yet from the standpoint of practicality the newer shock-proof roentgen ray tubes will accomplish much the same thing. I am using a shock-proof outfit which has cones varying in diameter from ¼ to 1 inch (0.6 to 2.5 cm.). The opening of the cone can be applied to the tonsil or to the dorsum or undersurface of the tongue, and those areas can be treated with 300 r per minute with a distance of 8 inches (18 cm.) between the anode and the mucous membrane. Such an outfit costs only about $900 to adapt to existing generators, whereas the Chaoul outfit costs $4,000. I wonder if either the adaptability of the Chaoul tube or some difference in the biologic action of the longer wave length compensates for the difference in price.

Dr. S. M. Kaufman, New York: I was not prepared to discuss Dr. Hollander's paper, but I feel that a few points have been brought out here that require further consideration. If an oral lesion is nonmalignant it can be removed without twenty treatments, as with the desiccating current in a few minutes. If the lesion is malignant and has already metastasized, I do not believe that daily irradiation for a month, as recommended by Hollander, will be of much value, even if the lesion does necrose and eliminate itself.

I feel that this form of treatment is similar to Bucky's grenz ray, which is a ray between a roentgen and a violet ray. A lesion in the mouth is serious, for even if it is nonmalignant in the beginning, it may become malignant at any time.

In cases in which the lesion is accessible, I prefer to remove it with a desiccating and coagulating current. In my opinion the result is much better than that following a form of treatment which requires daily irradiation for twenty days, without assuming cure of the condition.

Dr. H. R. Foerster, Milwaukee: My impression of this type of treatment is that it differs from the roentgen treatment customarily applied chiefly in the material reduction of the distance and therefore of the time of exposure, though both methods employ divided dosage.

I do not believe there is any difference in biologic action between roentgen rays applied at what amounts almost to contact and the same rays applied at a distance. There is certainly no difference between the biologic effect of the voltage Dr. Hollander uses with this apparatus and that of customary voltages that are somewhat higher.

In my own practice I use the same voltage as Dr. Hollander does (61 kilovolts) as a routine in therapy with unfiltered rays but higher voltages in therapy with filtered rays. In the treatment of intra-oral lesions in my office I have for many years used the regular roentgen equipment and a metal cone, on top of which a leaded glass cone can be attached. Leaded glass being an insulator and screen, the glass cone may be inserted directly into the oral cavity. This does not require a shock-proof tube or a special apparatus. The expense is probably the chief drawback of the Chaoul method.

There are, however, two distinct disadvantages to the type of cone that I have been accustomed to use: (1) The longer working distance increases the time of exposure and causes difficulty for the patient, who must hold the glass cone in the mouth for long periods; (2) with the introduction of an inflexible leaded glass cone into the mouth it is sometimes difficult to obtain the desired exposure. I have, however, effectively treated various types of intra-oral lesions on the tonsil, the tongue, the palate and the buccal surfaces.

I am of the opinion that in many intra-oral lesions either surface application of radium or the injection of radium emanation seeds or needles is preferable to the use of the roentgen rays, though I consider Dr. Hollander's research a valuable contribution. Further work along this line may prove this apparatus to be of value for institutional use if not for private practice.

Dr. Lester Hollander, Pittsburgh: I agree with everything Dr. Foerster has said. There is no difference in biologic effects between the various types of irradiation. I agree that no one needs to buy this apparatus. The important thing is not the apparatus but the direct introduction of roentgen rays into lesions of the mouth. The results that we obtained with the ordinary roentgen ray machine which we have been using since 1932 and with the contact therapy Chaoul tube are alike. As I stated in the opening paragraph of my paper, the big advantage is the reduced discomfort of the patient in holding his mouth open for from two to five minutes rather than from seventeen to forty-five minutes at a time.

Dr. Cipollaro and I have had a previous discussion on this question of massive doses. I believe that to maintain his supremacy in the treatment of intra-oral lesions the dermatologist must settle this question of a massive dose. In order to get a desired dose for epidermal carcinoma, which I think is never less than 18 units, an amount which I usually give in one week when I use the ordinary intra-oral type of apparatus, the physician punishes his patient a great deal. In getting the cumulative dose with the apparatus for contact therapy the patient is not punished. In a way, the Chaoul method of contact therapy is similar to the Coutard method of therapy, because the total dose is being built up by a certain dosage every day. Morison, Pendergrass and others believe there is great similarity between these two forms of therapy.

As far as benign lesions are concerned, I am of the opinion, possibly shared by others, that leukoplakia buccalis is far from being benign, and I believe that if I had the choice I should prefer a good pliable scar in my mouth to recalcitrant leukoplakia which had been attacked by all sorts of methods. Dr. Cipollaro says

this apparatus is not applicable to large lesions. I should like to contradict that, because we have treated carcinoma of the hard palate and the inside of the mouth that practically covered the mouth.

What I am principally interested in is the use of superficial roentgen radiation in proper doses within the mouth. Dr. Foerster was kind enough to answer Dr. Templeton's question, and I agree with his answer.

As far as Dr. Kaufman's remarks are concerned, I have no argument with him. If he wishes to use electrodesiccation to remove a lesion, that is good, and if he does not think these malignant local lesions should be treated in a way which will give the patient comfort, that is his own opinion.

As for the metastases, I deliberately did not mention them because this is a preliminary paper. Our patients all receive the usual treatment for involvement of the lymph nodes—massive doses of high voltage radiation—and I am so discouraged with the method that just two months ago we started an entirely new routine in such involvements, which briefly consists of complete and broad dissection of the lymph node-bearing areas in the cervical region.

631 Jenkins Building.

NAEVUS EPITHELIOMATO-CYLINDROMATOSUS

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CLEVELAND

The rarity of true turban tumor, benign epithelioma of the scalp or multiple cylindroma, is evident from the infrequent and diverse reports in the English literature. There have been but six reports in the literature of the United States since Cohn's [1] in 1892. When Ronchese [2] prepared his admirable article in 1932, there were but three reports. In addition to those of Cohn and Ronchese, there are those of Sutton [3] and Jones, Alden and Bishop,[4] Stillians' [5] two cases and the one Ormsby [6] presented before the Chicago Dermatological Society. The present paper deals mainly with the more common single cylindroma. In the past there have been serious difficulties in regard not only to the classification and terminology of these tumors but to their origin. Since the histologic appearance of this condition is characteristic, there should not be much difficulty in recognizing the nevus, provided biopsies are done as a routine and all tissues removed are studied microscopically.

DESCRIPTION

Clinically, cylindroma has usually been described as a multiple tumor occurring on the scalp. However, it is more often single, as illustrated by three of my four cases, and it may occur on the glabrous skin. The

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From the Department of Dermatology and Syphilology, Western Reserve University, School of Medicine, and the Lakeside Hospital.

Read before the Section on Dermatology and Syphilology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1937.

1. Cohn, I. E.: A Case of Multiple Sarcoma, J. Cutan. & Genito-Urin. Dis. **10**:393 1892.

2. Ronchese, F.: Multiple Benign Epithelioma of the Scalp, Am. J. Cancer **18**:875, 1933.

3. Sutton, R. L.: Diseases of the Skin, ed. 8, St. Louis, C. V. Mosby Company, 1931.

4. Jones, J. W.; Alden, H. S., and Bishop, E. L.: Turban Tumor or Sweat Gland Carcinoma, Arch. Dermat. & Syph. **26**:656 (Oct.) 1932.

5. Stillians, A. W.: Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, Arch. Dermat. & Syph. **27**:481 (March) 1933.

6. Ormsby, Oliver S.: Endothelioma Capitis (Turban Tumors) or Naevo-Epithelioma Adenoides (Hoffman), Arch. Dermat. & Syph. **32**:674 (Oct.) 1935.

tumors are of all sizes up to 4 or 5 cm. in diameter. They are round, bluish or pink and firm, and usually do not ulcerate. They appear in patients aged between 16 and 40 years and if not treated may continue their slow growth to a large size. Occasionally, along with the tumors of the scalp, a few lesions appear on other regions of the body. The incidence of the condition is greater in the female than in the male. It is hereditary and often affects several members of one generation. True turban tumor has been benign in all cases, even when of many years' duration.

When I came to investigate the reported deaths in cases of cylindroma, I found that Ancell's [7] patient died of an abdominal tumor which was probably not related to the tumors of the scalp. Sequeira's [8] patient died of cerebral hemorrhage, and it is not stated in the report whether the hemorrhage was due to local invasion by the tumor or to arteriosclerotic disease. Haslund's [9] case, which was reinvestigated by Frieboes,[10] was found to be one of malignant epithelioma which invaded the lymph spaces—certainly a different tumor from the one under discussion.

There is grave danger of making a wrong diagnosis if one labels as turban tumor any condition which shows rapid local growth and metastases. I observed one lesion which in clinical appearance resembled cylindroma, in that there had been a single slowly growing bean-sized nodule on the occiput for thirty years, but this was not a cylindroma. The lesion was injured, became infected and ulcerated. In spite of treatment by excision and roentgen irradiation, the entire left side of the head, the neck and the occiput became involved by a rapidly growing lobulated mass. In less than a year from the date of injury, the patient died of generalized metastases. Careful study of this malignant process revealed the same type of tumor cells in the scalp, the lymph nodes, the lungs and the liver, and the pathologic diagnosis of nevocarcinoma was readily made.

Malignant tumors of the scalp, unless their origin can be demonstrated from the benign basal cells of a typical cylindroma had best be excluded from this classification.

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7. Ancell, cited by Beck, S. C., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, p. 462.

8. Sequeira, J. H.: Diseases of the Skin, New York, The Macmillan Company, 1927, plate 52 B.

9. Haslund, P.: Multiple Endotheliome der Kopfhaut, Arch. f. Dermat. u. Syph. **82**:247, 1906.

10. Frieboes, W.: Atlas der Haut- und Geschlechtskrankheiten, Leipzig, F. C. W. Vogel, 1928.

HISTOLOGIC PICTURE OF CYLINDROMA

The histologic appearance of cylindroma is striking. Only borderline processes that present some of the features of benign cystic epithelioma and show hyalinization of the connective tissue are not readily labeled. Cylindromatous degeneration occurs in similar tumors of many tissues other than the skin, but this paper has been limited to a study of cutaneous cylindroma.

Sections from turban tumors and from single lesions on the scalp show a typical arrangement of basal cells in round, oval or elongated nests, packed closely so that the tumor is in almost solid lobules. The tumorous area in the corium is separated from the epithelium by a narrow band of normal connective tissue. The connective tissue around the tumor nests is degenerated into a dense hyalin sheath. In certain areas of the tumor, there may be "poured-in" hyalin within the cell masses. This "poured-in" hyalin appears as small masses of pink material, enclosed within actively growing epithelial tissue, and may be the result of degeneration of epithelial cells or of connective tissue.

The tumor cells stain deeply and have large round or oval nuclei, which are surrounded by a small band of cytoplasm. The outer one or two rows of cells have the palisade arrangement typical in basal cell epithelioma. The cells within the border row often begin to show signs of degeneration and cyst formation early in their course.

HISTOGENESIS

When one considers the origin of the turban tumor, one finds a great diversity of opinion in the literature. Jones, Alden and Bishop's [4] case suggested origin in the sweat glands, Ronchese's,[2] in the sebaceous glands and Stillians,[5] in the surface epithelium or the hair follicles.

The association of cylindroma with other nevoid proliferations is an established fact. For example, in Watanabe's [11] case and one of Stillians' cases this nevus was found in association with benign cystic epithelioma.

Schlammadinger [12] reported the case of a 36 year old woman with more than two hundred tumors on the face and the scalp. Histologic examination revealed that the tumors of the scalp were cylindromas and the smaller lesions on the face tricho-epitheliomas.

Biberstein,[13] working in Jadassohn's clinic, reported the case of a 34 year old man with ten small smooth red-brown masses on the scalp

11. Watanabe, J.: Ueber das Cylindrom und das Epithelioma adenoides cysticum, Arch. f. Dermat. u. Syph. **140**:208, 1922.

12. Schlammadinger, Josef: Cylindrom und Trichoepithelioma papulosum multiplex, Arch. f. Dermat. u. Syph. **171**:526, 1935.

13. Biberstein, H.: Epithelioma adenoides cysticum im Gesicht und Cylindrom am Kopf, Arch. f. Dermat. u. Syph. **142**:428, 1923.

and milium-like lesions on the face. Biopsy of each type of lesion was done. The tumors of the scalp were cylindromas, and the milium-like lesions were examples of epithelioma adenoides cysticum.

In Hoffman's [14] case cylindroma was associated with a mixed tumor of the parotid. Recent researches of Hoffman [15] led him to state the opinion that a close relationship exists between cylindroma and epithelioma adenoides cysticum. Cylindroma may originate not only in the epidermis but directly in epithelioma adenoides cysticum. Because of this, Hoffman suggested the term "adenoid-naevo-epithelioma" as the group name for both these nevi.

This coincidence, as well as the related origin, is best understood if one takes the fundamental point of view concerning the growth of the skin in the embryo aptly brought out by Dr. F. D. Weidman in his discussion of Stillians' [5] cases. He stated that although attempts have been made to classify dogmatically and precisely each nevus or nevo-epithelioma as originating from the sweat ducts, the pilosebaceous system, or the superficial epithelium, this cannot be done in many cases. Weidman stressed the importance of the embryonal factor in nevi. MacLeod,[16] in discussing the same feature, stated:

> It seems probable that they (cylindromata) are derived from groups of embryonic cells (cell rests of Cohnheim) which if they had fulfilled their developmental intention, would have developed into either epidermis, a pilo-sebaceous follicle, or a sweat gland, and that they belong to the class of naevi, and may be designated "naevi" cystepitheliomatosi.

I am of the opinion that the supposed diversity of origin of naevus epitheliomato-cylindromatosus has resulted from an over-zealous search for a single cell origin for each cylindroma, the fact of its deviation from an undifferentiated ectoderm being lost sight of.

REPORT OF CASES

In the past three years an opportunity has been afforded me to study four cases of this disease:

Case 1.—Mrs. J. J. N., a white woman aged 30, reported to Drs. Cole and Driver on March 6, 1934, with a single raised lesion 16 mm. in diameter on the vertex of her head. It was firm and reddish. There were some small vessels on its surface. The duration was seven years.

The lesion was totally excised, and the base was cauterized. The wound healed rapidly, and there has been no recurrence at the time this report is written.

Microscopic Examination (fig. 1): The epidermis was thin and showed slight hyperkeratosis. It showed no connection with the tumor cells in the corium.

14. Hoffman, E., cited by Frieboes.[10]

15. Hoffman, E., cited by Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1928, vol. 2.

16. MacLeod, J. M. H.: Diseases of the Skin, New York, Paul B. Hoeber, Inc., 1921.

There was a definite band of free connective tissue slightly infiltrated with lymphocytes between the epidermis and the nests of cells. Throughout the corium were round or elongated collections of cells which were closely packed. Most of the nests were surrounded by a dense hyalin sheath or cylinder.

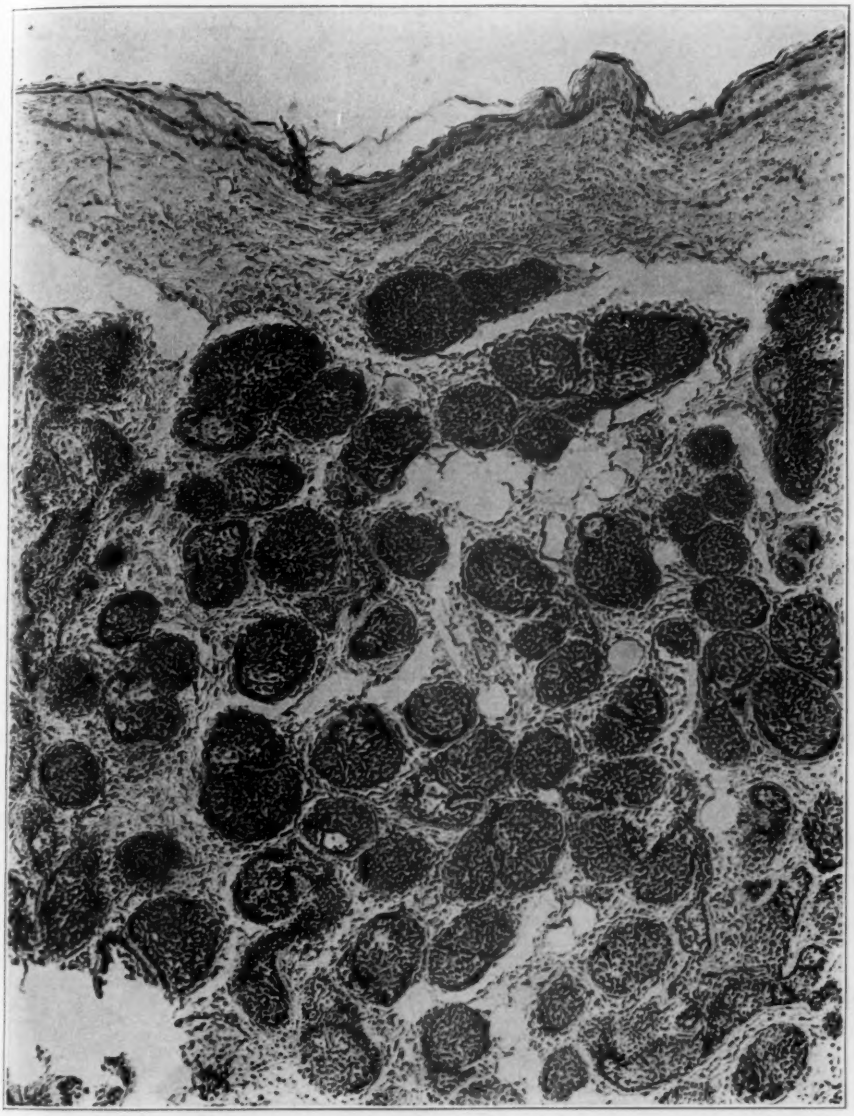

Fig. 1 (case 1).—Low power magnification of tumor deep in the corium and separated from the epidermis by normal connective tissue. Cystic spaces appear within the cell masses.

The outer row of cells stained more deeply than the central cells. They were columnar and showed dark-staining nuclei. They were arranged in a palisade manner.

The nuclei of the central cells were oval, had little cytoplasm and resembled nevus cells. About 50 per cent of the cell masses, usually those with a dense hyalin ring, showed cystic spaces, filled with degenerated cells. The larger cell masses were studded with rods of "poured-in" hyalin.

The diagnosis was naevus epitheliomato-cylindromatosus.

CASE 2.—Miss E. B., aged 25, came to her physician[17] on Sept. 15, 1931, because of a "wen" just above the hair line on the forehead. She reported that she had had three similar, nonulcerated lumps excised from her scalp one year before. The tumor complained of at this time was 15 mm. in diameter, ulcerated, infected and bleeding. In addition to this tumor, an examination showed nodules varying in size from that of a match head to 5 mm. distributed irregularly over the entire scalp. They were firm, but not hard, and pink. Altogether there were about forty nodules, and when the patient was last seen there was a large nodule within the pinna of the left ear.

An interesting family history was obtained from the attending physician's notes: Her sister, Mary B., aged 41, had several small tumors in her scalp in front of each ear in February 1933. In April 1934 the growths on the scalp were much larger and more tumorous, and in February 1935 the lumps in the scalp were certainly larger than they had been at any time—were probably cylindromas. On Sept. 29, 1935, around the forehead there were more cylindromas, and in the vertex of the scalp there was a nodule, probably cylindroma, the size of a hickory-nut. None of these tumors of the scalp were excised.

A third member of the family, Mrs. J. W. B., mother of E. B. and Mary B., was seen on June 10, 1933. She said she had had several lumps on her scalp for years. There were three tumors from 1 to 2.5 cm. in diameter on her scalp; the largest was infected and bleeding. There were scars of two former infected tumors, which had disappeared without treatment. The physician excised the infected, bleeding tumor on the same day, and the wound healed uneventfully. The pathologic report stated that this neoplasm was essentially similar to those of E. B., except that the cylindromatous architecture, which might have been present in the deeper nodules, was not evident in the tissue examined.

Microscopic Examination of Tissue from E. B.: The epidermis was atrophic and thinned, and the rete pegs were flat. Within the corium at all depths were numerous small and large nests of cells which were either round, oval or spindle shaped. The nuclei were proportionately large and stained darkly. They were arranged without any suggestion of polarity. The border range of cells were basal cells. Interspersed throughout the cell masses, and to a mild degree surrounding the masses, were well defined hyalin bands.

The sweat glands appeared normal. From some of the sebaceous glands there were solid prolongations of cells showing disturbances of polarity and closely resembling those of the tumors.

The diagnosis was naevus epitheliomato-cylindromatosus.

17. Dr. R. Reyburn McClellan, of Xenia, Ohio.

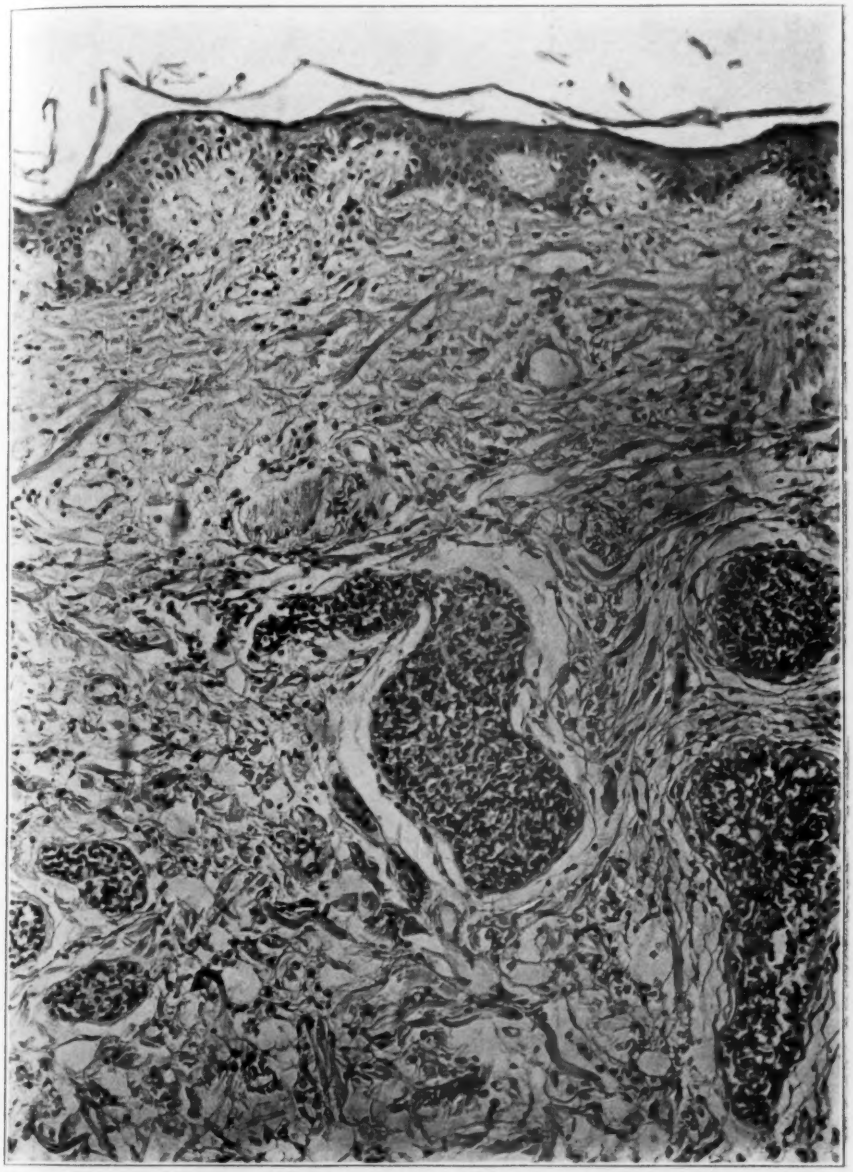

Fig. 2 (case 2).—Low power magnification of small cylindroma nests in the subpapillary layer of the corium.

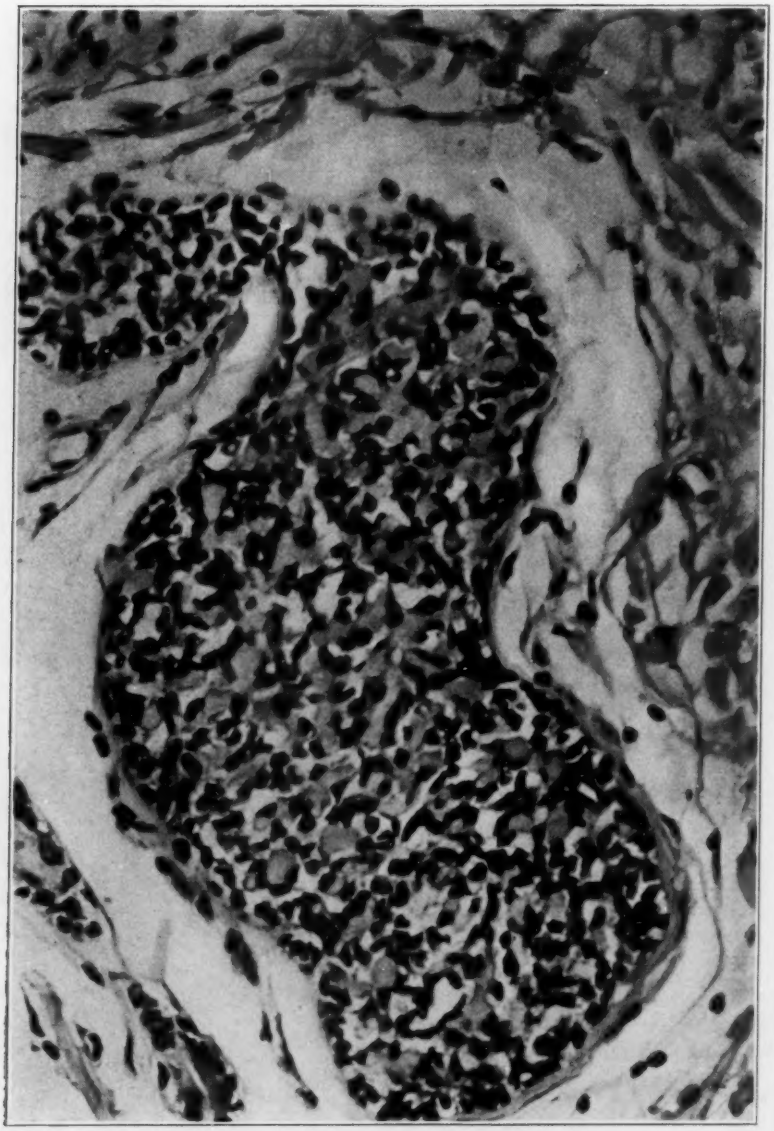

Fig. 3 (case 2).—High power magnification showing the uniform character of the small basal cells, an incomplete hyalin sheath below and the degeneration of hyalin in the cytoplasm of the cells. The nuclei remain intact, compressed by dense hyalin.

CASE 3.—Mr. T. D., aged 66, complained of a small tumor on the left parietal region of the scalp of twenty years' duration. It had enlarged slowly to the size of a walnut and was not painful. Recently he had accidentally traumatized the tumor and produced annoying and recurring hemorrhage. Since then, and possibly as a result of this trauma, the tumor had rapidly increased (fig. 4).

In the left parietal region of the scalp there was a light reddish tumor with a broad base, which measured approximately 2.5 by 2.5 by 3 cm. The top of it was crusted over. It was firm, and manipulation tended to start bleeding in the crusted part. There were no remarkable lymph nodes.

Microscopic Examination: Biopsy revealed that the tumor was made up of large and small sharply circumscribed masses of cells of the basal type. Within the cell masses the outlines of the cells were indistinct, but at the periphery the cells were radially disposed and formed a sharp barrier between the tumor and the stroma. A striking characteristic of the tumor was the formation of alveolar

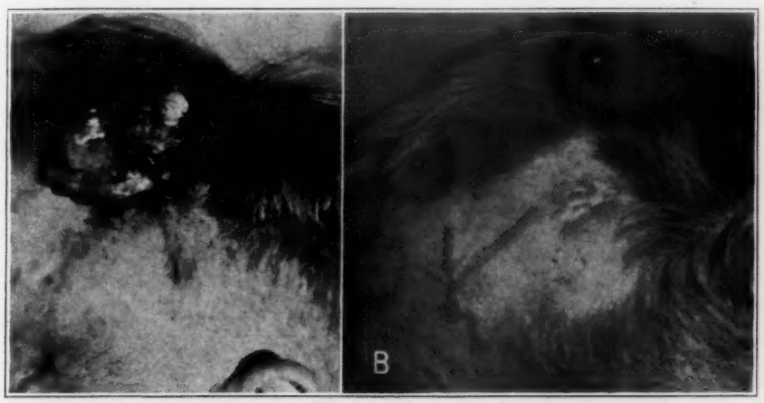

Fig. 4 (case 3).—*A*, tumor mass before therapy; *B*, appearance after treatment by excision and radium puncture of the base.

or cystic spaces of varying sizes. Where the latter appeared, tumor cells frequently formed projecting nodules within the cyst. The degree of organization varied, and, although solid masses of basal epithelioma cells characterized the tumor, there were several situations in which these solid masses had been broken down by hemorrhage or by ingrowth of the stroma. In some places the stroma was richly vascularized, and in others it was densely cellular and even hyalinized. The tumor cells had scanty cytoplasm and relatively large round or oval chromatic nuclei. There was little nuclear variation.

The diagnosis was naevus epitheliomato-cylindromatosus.

CASE 4.—Mrs. H. D., a white woman aged 58, came to Drs. Cole and Driver complaining of a lump in the canal of her left ear of six months' duration.

Her daughter, aged 36, gave a history of having a "sebaceous cyst" removed from the vertex of her scalp at the age of 33 years.

An examination showed a smoothly rounded nodule 1 cm. in diameter firmly embedded in the subcutaneous tissue over the cartilage of the outer, inferior portion of the left auditory meatus. The skin over the nodule was perhaps a little reddened but was almost normal in color. This was the only lesion found on the skin or the scalp.

The nodule was excised, and the area was cauterized. Healing was rapid, and there has been no recurrence.

Microscopic Examination: The section revealed a slightly flattened but otherwise normal epithelium over the nests of tumor cells. There was the usual well vascularized band of connective tissue between the epidermis and the uniform masses of basal cells filling the corium. All the cell masses were surrounded by a complete, thick and dense hyalin sheath, and many were penetrated by long icicle-like rods of hyalin. (These rods were the vinelike threads which Stillians [5] described in his case 1.) The tumor cells were small and basal and in this case seemed to reproduce in part sebaceous glands. Cystic degeneration was absent.

The diagnosis was naevus epitheliomato-cylindromatosus.

COMMENT

Since 1900 the literature on cylindroma has been somewhat more uniform in regard to both nomenclature and material, in that with a few exceptions the authors have been reporting true cylindromas.

Investigation of the cases reported by Ancell, Haslund and Sequeira, in which there had been some doubt about the diagnosis, showed that the death of each patient was either not due, or could not be attributed directly, to the presence of cylindroma.

Microscopic examination of these four cylindromas showed no evidence of malignancy. The tumors were usually well encapsulated, did not invade the lymphatic vessels and were not remarkable for mitoses. I have not observed or found reported a single case in which the regional lymph nodes were involved. Since the lymphatic vessels are not involved, it follows that widely separated multiple lesions in cases of turban tumor must arise from multiple points of origin and are not disseminated from a single lesion. I agree with Ronchese that malignant growths should be excluded from the category of cylindroma.

The spontaneous disappearance of some ulcerating cylindromas, as in the mother in case 2, is interesting. This was observed many years ago by DeBeurmann.[18] He was the first one to use radium in the treatment of cylindroma.

Although I am aware that the literature gives a preponderance in incidence to the more striking turban tumor, my experience in observing three single cylindromas in Cleveland while I had access to but one case of turban tumor leads me to believe that the routine histologic study of all cutaneous tissues will reveal that singular cylindroma is more common than turban tumor. Lemaitre's [19] studies indicated that single

18. de Beurmann, H.: Cylindroma, in Neisser, A., and Jacobi, E.: Ikonographia dermatologica, Berlin, Urban & Schwarzenberg, 1910.

19. Lemaitre, Y.: Étude anatomo-clinique des tumeurs dites cylindromes, Paris, Vigot Frères, 1936.

cylindroma of the skin is a more frequent clinical type. Savatard [20] has had precisely this experience with epithelioma adenoides cysticum, the so-called multiple benign cystic epithelioma.

In cases 1 and 4 reported here excision and cautery alone effected cure. In case 3 the lesion responded to excision and interstitial irradiation of the base. In case 2 individual nodules responded to excision but not to therapy with filtered roentgen rays.

SUMMARY

Four cases of cutaneous cylindroma, their histologic picture, and their treatment are described.

When the deaths in reported cases of cylindroma were investigated, they could not be attributed to the cylindroma. There have been no recent reports of malignancy in this condition.

As with benign cystic epithelioma, such tumors are more commonly single than multiple. Turban tumor is an infrequent manifestation of cutaneous cylindroma.

Naevus epitheliomato-cylindromatosus is benign throughout its course, even when of many years' duration, and is cured by the simple procedure of excision.

227 Carnegie Medical Building.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: One of the practical applications of this paper lies in the fact that whenever apparently carcinomatous tumors of the scalp are seen examination should be made of other parts of the head, particularly of those areas common to the distribution of multiple benign cystic epithelioma—that is, the angles of the nose, the corners of the mouth, the middle of the chin and, what I think is commonly not emphasized enough, the position immediately in front of the ear. Numbers of small lesions pass as ordinary pimples and go unnoticed on account of their size, and as soon as one of these tumors of the scalp is met with, whether it is the larger expression, namely, the true turban tumor, or an expression like those just described, particular attention should be paid to the positions I have just enumerated, which are along the lines of embryonal closure.

There is a particularly cogent item in this presentation, namely, that one of the lesions was found springing from an accessory lobe of the ear. This brings forcibly to attention the nevic connections in what are essentially multiple benign cystic epitheliomas. Some are extremely multiple, such as those illustrated in dermatologic textbooks, with hundreds of lesions; others are present in smaller numbers—maybe only ten or a dozen—and finally there are examples, such as those presented, of "solitary multiple" benign cystic epithelioma, paradoxical as it may sound.

"Cylindroma," as I see it, is the appropriate term for the more complex forms of tumors with the hyaline features of this classification. I came prepared to agree

20. Savatard, L.: Epithelioma Adenoides Cysticum, Brit. J. Dermat. **34**:381, 1922.

entirely with Dr. Binkley, but since he has shown the slides on the screen, I feel that some of the tumors were not cylindromas. In some of them it was difficult indeed to see any hyalin around the lesions. I might say that the general pathologist today is frowning more and more on the use of the term "cylindroma." It suggests simply a morphologic picture and does not express anything biologic. It is better to speak of these tumors of the scalp as tricho-epitheliomas, which so many of the multiple benign cystic epitheliomas are.

Dr. Richard L. Sutton Jr., Kansas City, Mo.: I reported a case three years ago (Arch. Dermat. & Syph. **30**:195 [Aug.] 1934) that fits into this group, although I called the condition syringocystadenoma nodularis, believing that it arose in the sweat gland anlage. It was limited to one side of the body and was distributed in nodules similar to those that Dr. Binkley described, reaching from the region of the vertebra prominens around the neck to the anterior midline. I postulated its origin in the sweat glands on the facts that the tumor was, histologically, of two-layered epithelial-cylindric structure, with considerable proliferation of the cells of the outer layer and that less highly evolved nodules of syringocystadenoma were present beside and superficial to the larger nodules. Parts of the masses were cystic, and in places there were deposits of cholesterol. Many authors have expressed the belief that turban tumors originate in the sweat glands.

Many tumors of the scalp are, of course, sebaceous cysts, and when they become malignant they are almost invariably squamous cell carcinomas.

Biopsy specimens should not be removed from tumors of the scalp, but the whole tumor should be excised promptly and the pathologist's work done afterward. It must be taken out in order to be got rid of.

Dr. George W. Binkley, Cleveland: The terminology in regard to these tumors was an interesting stumbling block. There are no less than thirteen names for the condition in the literature, and in my survey I found that the term tricho-epithelioma was used as almost synonymous with epithelioma adenoides cysticum. However, since there is such a close relationship between epithelioma adenoides cysticum and cylindroma, I for one would be willing to subscribe to that generic term to include both conditions.

The histogenesis was a difficult problem, and I decided not to spend too much time on it. I may say, however, that the lesion that occurred in the ear of the woman had its most marked hyalinization around the nests of basal cells and projecting in icicle-like rods within each cell nest were hyalin rods. This tumor appeared to be derived from or looked most closely like material from the sebaceous glands. In the last case the condition was somewhat different. The tumor there seemed to be derived from hair follicles.

MELANOMA CAUSED BY INDELIBLE PENCIL

HERMAN SHARLIT, M.D.
NEW YORK

Aniline and its derivatives and coal tar, their natural mother substance, have demonstrated their ability to produce inflammatory and neoplastic reactions in the skin. In a special class in this category of cutaneous reactions are those in which the skin and adjacent subcutaneous tissues are impregnated with derivatives of aniline from an indelible pencil. The accident of piercing the cutaneous surface with an indelible ink pencil and of breaking off in the tissue of bits of the ink substance is not rare. Abundant records [1] of such accidents speak for this, as well as for the repeatedly similar course of the reaction to the substance. Intense inflammation and resulting necrosis and fluidification of the involved tissue are the invariable stages which lead to ulceration, extrusion of the foreign dyes via the exudate and ultimate but sluggish healing. Naturally, the amount and the depth of the impregnation and the degree of dispersion of the dye in the tissue determine the severity of the reaction.

Not infrequently the original injury is merely a stain just beneath the epidermis, similar to that effected by stroking a pencil across a paper. One can readily understand how much a "tattooing" might remain innocuous indefinitely, and one may safely assume that this frequently happens, leaving no justification for medical recording. After such an episode as this and after approximately four years of latency there ensued at the site of the "tattooing" the sequela that is the subject of this report. That the history of tattoo with indelible ink pencil may be considered reliable, I shall say that I observed the patient at frequent intervals for about two years (preceding the onset of this condition) for an unrelated condition and that at one of the earliest visits I remarked about this nevus-like spot. I was then advised by both parents of its nature. The details of this trauma were vivid, clear and certain in the minds of both parents, and their insistence on the correctness of the story in spite of all doubts expressed by the consultants at the time of the onset of the sequela herein reported must leave one with a feeling of certainty as to its correctness. At least it

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Read before the Section on Dermatology and Syphilology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1937.

1. de Puoz, John: Schweiz. med. Wchnschr. **63**:1124 (Nov. 4) 1933.

is a detail of history given to me *ante hoc* and free from the unreliability of retrospective history elicited under the emotional strain of impending disaster.

REPORT OF A CASE

A white boy aged 9½ years had been seen frequently by me for over two years for advice about hereditary keratosis of the palms and the soles. At one

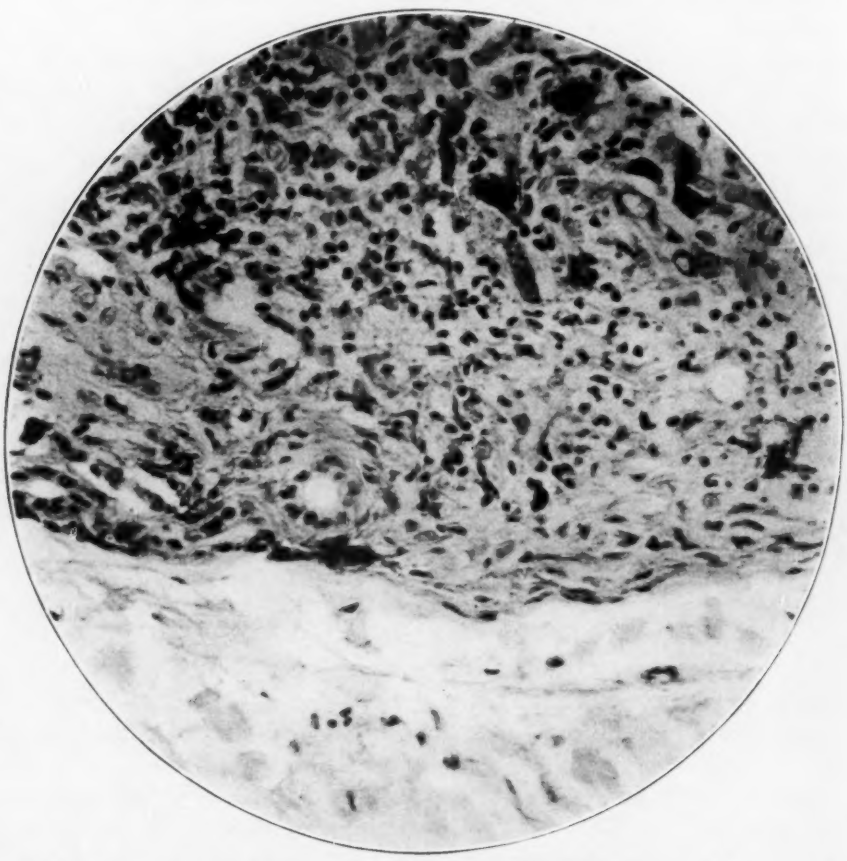

Fig. 1.—Section of the growth showing evidence of inflammatory features of the tumor.

of the earliest of these consultations I had noted in the middle of the forehead a bluish discoloration the size of a pencil point. The parents then had ascribed it to tattooing with an indelible pencil some time before. When I saw the patient in December 1933 I observed that the "blue spot" was distinctly brownish, had enlarged to about 0.6 cm. in long diameter and was definitely elevated. The parents stated that the "spot" had been "developing" for at least two months. Within a week the mass was surgically excised, and the wound was healing by primary intention. No other treatment was given. Approximately three and one-half years later (April 1937) there were no known sequelae.

Histologic sections of this growth were carefully studied by five pathologists. The chief point of interest was the failure of the pathologists to agree on the fundamental fact of the neoplastic or the inflammatory nature of this growth. I give in full only Dr. Alfred Plaut's report as originally submitted Dec. 11, 1933, and as supplemented by his report of May 29, 1934, since his report covers the conflicting opinions and the chief arguments for each:

"Report on Cutaneous Specimen from Forehead, Submitted on December 11, 1933.—Thick masses of pigment occupied a large area in the cutis, in some of the

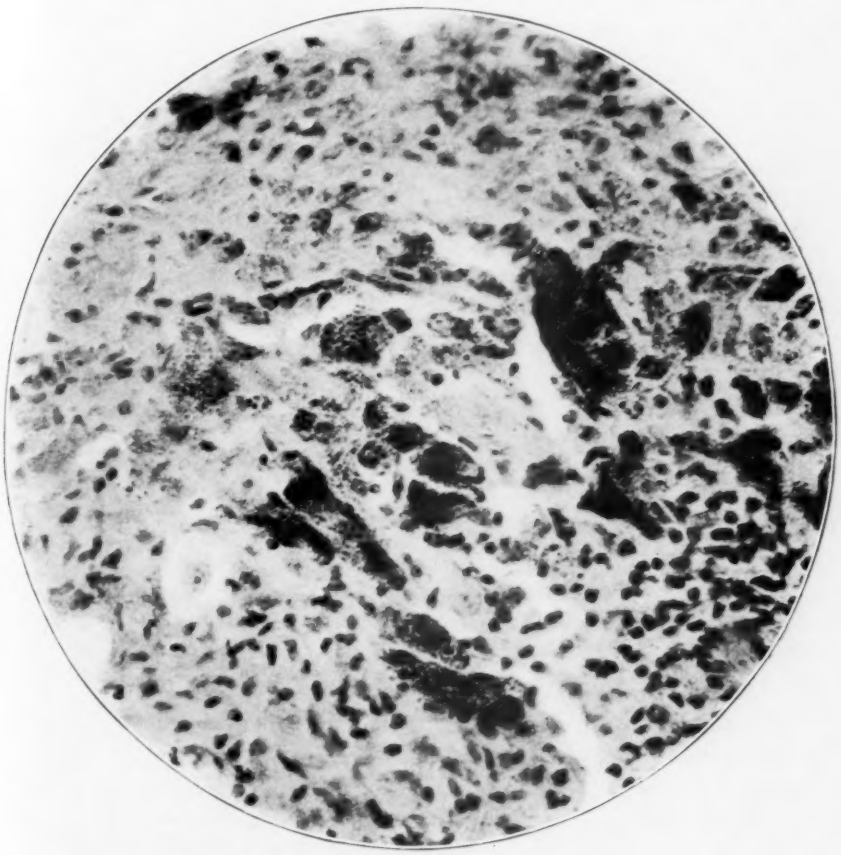

Fig. 2.—Section showing large cells containing melanin.

sections reaching high up into the corpus papillare. The pigment gave all the chemical and staining reactions of melanin, silver nitrate, compound solution of iodine, carbolfuchsin and polychrome methylene blue being used. There was a negative reaction for iron. After being bleached with potassium permanganate and oxalic acid, the pigment-containing cells appeared partly as irregularly elongated elements and partly as large round or ovoid cells, with rather clear, round nuclei. Dendritic forms were seen occasionally. Between the pigmented cells many small, dark nuclei were situated. These were obviously inflammatory. There were, how-

ever, hardly any leukocytes or plasma cells. No *Mastzellen* were seen. The pigmented cells formed distinctly outlined large masses in the deeper layers of the cutis. In one portion of the specimen this formation predominated. In other portions, however, less distinctly outlined accumulations of pigmented cell occupied the upper layers and at several points reached the surface epithelium. In these regions pigmented cells were seen lying close to the basal layer. While the pigment of the surface epithelium itself appeared normal throughout the specimen, the presence of pigmented cells in the immediate neighborhood was conspicuous over the lesion, and such cells were absent in the normal portions of the section. Careful examination revealed changes in the basal layer. There were large, round, clear cells, some of which were situated within the basal layer, while others, singly or in groups, were situated directly below it (acantholysis or *Abtropfung*). No foreign bodies were observed, and there was no foreign body reaction. The fibers of the cutis in places were almost completely destroyed. Whether this destruction was due to an inflammatory process or not could not be decided. The diagnosis was malignant, probably epithelial melanoma."

"Additional Comment on Section of Tissue, May 29, 1934.—The specimen was received together with the history that the boy had injured his forehead some time before with an indelible pencil. On first examination the unusually sharp outline of the lesion seemed to correspond well with a history of trauma. As examination progressed, however, the idea of a traumatic inflammatory lesion was given up, and a diagnosis of malignant melanoma was made (see original report). One expert on tumors to whom the slide was shown concluded after some hesitation that the condition was a benign melanoma. Another experienced pathologist at once excluded a diagnosis of tumor and considered the condition to be one of pigmentation with melanin secondary to an old inflammatory lesion."

This last diagnosis is certainly consistent with the aforementioned sharp outline of the lesion and with the clinical history. I could not have made this diagnosis, because I have never seen melanotic pigmentation secondary to an inflammation. I have been told, however, that this association does occur. Several details of the microscopic picture could be used in favor of the one or the other diagnosis. The large nonpigmented cells, for instance, with large pyknotic nuclei, could be explained more easily on the basis of tumor than of inflammation. The fact that the sweat glands were completely surrounded by the lesion but not destroyed is more compatible with the diagnosis of a chronic inflammation.

I could find no record in the dermatologic literature of a solitary melanotic inflammatory tumor. The extensive literature on injury to the skin by indelible pencil reveals no record of melanotic tumor. While uncertainty must necessarily persist as to the inflammatory or the neoplastic nature of the tumor described in this report, there should be no hesitancy in accepting impregnation of the skin with a derivative of aniline as the essential factor in its causation. The unusual opportunity to check this feature of the history, particularly at a time when the sequela recorded herein had not yet appeared, stamps this history as unequivocally reliable.

Derivatives of coal tar both natural and synthetic, are known to be carcinogenic. Their relationship to cutaneous melanosis is recorded in many reports on melanoderma in workers with tars and oils. A patient's history of growth in a melanotic spot on the skin or a request for

removal of a nongrowing pigmented nevus continues to arouse professional funk in the dermatologist and leads to judgments and practices reflective chiefly of the dermatologist's own attitude toward life. If it is borne in mind that the histopathologist when issuing a prognosis for cutaneous melanotic tumor is the Cassandra of medicine (a prophet whose oracular statement we may often justly ignore); that no evidence exists that metastatic melanosis has been directly precipitated by surgical excision of a solitary melanotic tumor or nevus from the skin and that if the melanosis has already extended aid even by radical amputation is impossible, a simple, unemotional attitude toward this almost daily problem of the dermatologist would prevail.

A melanotic lesion that shows evidence of growth or one that a patient seeks to have removed for cosmetic reasons should be surgically removed. In the present state of knowledge of the subject this removal should be the alpha and the omega of the treatment. A physician should not consider it necessary, with or without the help of a histopathologist, to frighten patients or members of their families by ominous insinuations. Failure to practice this rational routine of excision carried the parents of this boy through a terrifying week, while pathologists reported malignant and then benign melanoma and finally simple inflammation with pigmentation. The potentialities of cutaneous melanoma are still of only academic interest, since nothing can be done with certainty either to avoid metastases or to induce them.

SUMMARY AND CONCLUSION

A report is made of a growing melanoma in a child at the site of an indelible pencil tattooing of the skin some four years before the onset of the growth. The removal of the tumor by excision gave histopathologists an opportunity to differ as to the potentialities of this growth.

It is suggested that growing melanotic tumors or melanotic nevi which are cosmetically objectionable should be surgically removed without any further procedure, since malignant sequelae cannot be anticipated or prevented.

ABSTRACT OF DISCUSSION

DR. S. W. BECKER, Chicago: This able presentation brings up many points relative to melanotic tumors. These blue spots are usually blue nevi or tattoos, often from stabs with the point of a pencil or a pen.

The differential diagnosis depends on the history of trauma and the presence of a tiny scar over the lesion. If the lesion is due to a foreign body, one usually finds foreign material along with a foreign body granuloma in the section. None was present in this section, although the aniline dye may have been more or less soluble and may have disappeared.

The history of the lesion's becoming brownish definitely takes it out of the class of ordinary tattoo, because tattoo lesions do not become brownish unless superficial melanosis has occurred.

There is no inflammatory lesion of any type that contains as much melanin as this particular tumor shows on the lantern slides. I believe that one can make a diagnosis of malignant melanoma from the lantern slides. The degree of malignancy, however, varies tremendously and cannot be determined even from the sections.

Some years ago I endeavored to produce melanoma by injecting scarlet red dissolved in olive oil into the ordinary house or field mouse. I applied crude coal tar, which has known carcinogenic properties, in the same way. Unfortunately, the mice died from intercurrent infection before any neoplasm could develop. Dr. M. J. H. Grand, of New York, has cultured tissue from a melanotic sarcoma from the mouse, but to my knowledge repeated melanoma formation from any type of carcinogenic substance, aniline dye or other, has not occurred. I trust that I shall have an opportunity to see the sections, and I may modify my discussion accordingly.

Dr. Herman Sharlit, New York: One thing is certain about this case, and that is the history. An indelible pencil traumatized the skin, the trauma being evidenced by a tattoo mark; subsequently a growth occurred on the site of this tattoo mark. What is uncertain is the nature of the tumor. The pigment therein is unquestionably melanin. There was no expectation of finding the dye; it was anticipated that alcohol would dissolve all of it. It is unfortunate and unfair to Dr. Becker that he had no opportunity to see the slides. This was no fault of mine or of his.

The case is entitled to recording under the title I have given it, irrespective of the nature of the tumor, for the condition is the result of damage to the skin and the subcutaneous tissue from an indelible pencil. While no such reaction has been reported previously, this does not, in my mind, in the slightest militate against the truth of the relation of this growth to damage by indelible ink to the skin as herein reported.

Minor Notes

TREATMENT OF IMPETIGO CONTAGIOSA WITH COMPOUND CHLORHYDROXYQUINOLINE OINTMENT

C. C. Carpenter, M.D., Summit, N. J.

The success of treatment of sycosis vulgaris with compound ointment of chlorhydroxyquinoline indicated that the preparation might be valuable in the therapy of impetigo contagiosa. In cases of both infections Staphylococcus albus has been isolated and partially blamed, though according to Sabouraud the streptococcus is the cause of the disease under discussion.

It is generally conceded that any effective drug must be antiseptic and in a concentration of such strength that the normal surrounding skin is not injured. There should be no existing dermal hypersensitivity to the drug to be used. The compound ointment of chlorhydroxyquinoline can be used in sufficiently weak concentrations to comply with the second condition. As it has not been used as extensively as the mercurial antiseptics, it is believed that there is less possibility that hypersensitivity will be encountered.

To investigate its action two groups of cases were selected in which the preparatory treatment had been similar. In one group an ointment containing 2 per cent ammoniated mercury was used every four hours, and in the other an ointment containing 0.25 per cent chlorhydroxyquinoline and 5 per cent benzyl peroxide in equal parts of hydrous wool fat and white petrolatum was employed. The time necessary to arrest the activity of the infection and to regain a normal dry epithelium was observed to be as follows:

Therapy	Number of Cases	Age of Subjects, Years	Healing Time, Days	Cases of Dermatitis from Therapy
2% ammoniated mercury ointment	25	6-45	5.0	2
Compound chlorhydroxyquinoline ointment	25	3-52	4.7	1

From the table it may be seen that the recommended ointment compares favorably in results obtained with an ointment of ammoniated mercury and that there is less possibility that dermatitis may be produced.

Summit Medical Group,
129 Summit Avenue.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

PURPURA HAEMORRHAGICA WITH LYMPHOCYTOSIS: AN ACUTE TYPE AND AN INTERMITTENT MENSTRUAL TYPE. G. R. MINOT, Am. J. M. Sc. **192**:445 (Oct.) 1936.

Minot describes three cases of acute purpura haemorrhagica in which head colds preceded by two weeks the purpuric lesions. An increase in lymphocytes was found in the blood, and many of these lymphocytes were abnormal. All the patients recovered.

He reports three other cases in which the condition occurred in association with menstruation. The attacks varied from three to seven in number and ceased spontaneously. Fever accompanied some of the temporary increases in lymphocytes.

JAMIESON, Detroit.

GENERAL PARESIS TREATED BY MOSQUITO-INOCULATED VIVAX (TERTIAN) MALARIA. ERNEST KUSCH, D. F. MILAM and W. K. STRATMAN-THOMAS, Am. J. Psychiat. **93**:619 (Nov.) 1936.

Better results were obtained with malaria therapy when the patient was infected directly by a mosquito bite than when he was inoculated with infected blood. A strain of the mosquito infected with tertian malaria (Plasmodium vivax) was cultured for this purpose. The malaria so induced has an incubation period of from eleven to fourteen days, and about half the patients had spontaneous remissions. The others responded promptly to quinine. Because the mosquito-induced malaria is milder than the blood-produced form, it is possible to allow more chills and to secure better clinical results. Thus, in a series of patients with blood-inoculated malaria the number of paroxysms per patient varied from 8 to 12. In the group of patients bitten directly by the mosquitoes the number of paroxysms varied from 17 to 24. Similarly, the proportion of remissions was 19 per cent for the blood-inoculated group and 26 per cent for the mosquito-infected group. In the former group 7 per cent of the patients died, presumably from the malaria. None of the mosquito-infected patients died. The proportion who improved or who reached a remission totaled 75 per cent in the series of patients who were bitten directly by the insect and only 55 per cent in the blood-inoculated group. The authors conclude that when proper facilities are available the treatment of dementia paralytica with malaria induced by mosquito bite is the technic of choice.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

THE EFFECT OF TRYPARSAMIDE ON THE EYE: A CLINICAL STUDY OF THE OBJECTIVE OCULAR REACTION. L. L. SLOAN and A. C. WOODS, Am. J. Syph., Gonor. & Ven. Dis. **20**:583 (Nov.) 1936.

A study was made of sixteen patients who showed, after tryparsamide therapy, an objective ocular reaction, with definite changes in the visual fields. Prior to treatment all the patients had normal optic nerves and visual acuity and fields.

Two types of objective reaction, acute and chronic, occurred. The acute type, which is rare, is characterized by rapid loss of vision, reaching almost complete blindness. Only one of the authors' sixteen patients showed an acute reaction. He became almost blind within three days after the first injection, but after forced spinal drainage the fields and vision returned almost to normal eight months later.

The chronic reaction is characterized by contraction of the visual fields, with retention of normal central vision and absence of objective signs of atrophy of the optic nerves. There is a marked tendency toward gradual recovery from the defect in the fields if tryparsamide therapy is discontinued.

In two cases in which tryparsamide therapy was continued, atrophy of the optic nerves developed. One patient reached complete blindness. One patient had normal central vision and moderate contraction of the fields, which remained unchanged during the two year period of observation after cessation of tryparsamide therapy.

In cases involving both chronic and acute objective reactions a characteristic defect in the visual fields, as determined by a 1 degree white test object, manifested itself as a contraction chiefly in the upper, lower and nasal portions of the peripheral field.

The sensitivity to light of the central retina is reduced in patients showing a severe reaction with marked contraction of visual fields. In reactions of moderate severity, the central sense of light is usually unaffected.

For patients with normal optic nerves, fields and vision prior to the use of tryparsamide, there is little danger of any serious ocular damage, provided the drug is permanently discontinued at the first appearance of defects in the visual field. Continued administration of the drug, however, may result in serious visual damage or in complete blindness.

TEN YEARS' EXPERIENCE WITH MALARIA IN NEUROSYPHILIS. U. J. WILE and E. A. HAND, Am. J. Syph., Gonor. & Ven. Dis. **20**:630 (Nov.) 1936.

The authors report on 474 patients with neurosyphilis treated by induction of malarial paroxysms. The observations extended over a ten year period.

Encouraging results were noted in dementia paralytica, in the control of certain symptoms of tabes dorsalis, in diffuse cerebrospinal syphilis, in asymptomatic cerebrospinal syphilis and in acute basilar meningitis. Juvenile dementia paralytica was in no way benefited by malarial treatment. The types of cases with the best apparent prognosis are those with acute onset and those with some background of treatment prior to the onset of cerebrospinal symptoms.

Patients with dementia paralytica, as well as those with tabes, in whom there are marked destructive processes of the brain and the spinal cord, are not benefited, nor are the symptoms of degeneration retarded.

Encouraging results have been recorded, consisting of occasional retardation or arrest, in cases of atrophy of the optic nerve.

There is no striking parallel between clinical improvement and the serologic reactions of the spinal fluid and the blood.

THE EFFECT OF IODOBISMITOL UPON SPINAL FLUID FINDINGS IN EARLY SYPHILIS. G. S. JOHNSON and C. W. BARNETT, Am. J. Syph., Gonor. & Ven. Dis. **20**: 651 (Nov.) 1936.

It has been suggested that iodobismitol, with saligenin, because of its increased penetration of the meninges, might prevent involvement of the central nervous system in early syphilis. The authors report on the incidence of involvement of the central nervous system, as evidenced by abnormalities of the spinal fluid, in 120 patients with primary or secondary syphilis. Each patient had received at least 20 injections of iodobismitol with saligenin in addition to neoarsphenamine or mapharsen, prior to examination of the spinal fluid.

The incidence of abnormalities in the spinal fluid was 13 per cent, a figure practically identical with that reported for other patients with early syphilis who were given continuous treatment with arsphenamine and either bismuth or mercury but no iodobismitol.

The authors conclude that the substitution of iodobismitol with saligenin for other heavy metal preparations in the routine treatment of patients with primary or secondary syphilis does not eliminate the problem of involvement of the central nervous system.

THE SIGNIFICANCE OF FUSOSPIRILLOSIS IN GENITAL LESIONS: A COD LIVER OIL GLYCERIN NEOARSPHENAMINE METHOD OF TREATMENT. R. B. GREENBLATT and J. C. WRIGHT, Am. J. Syph., Gonor. & Ven. Dis. **20**:654 (Nov.) 1936.

Many of the chronic, rebellious lesions of the genito-anal region are complicated by superimposed fusospirillosis, which requires treatment irrespective of the underlying lesion. Intravenous infusions of arsenical drugs give little or no benefit in this secondary infection. In the acute gangrenous phagedenic ulcer instant assault on a virulent strain of fusiform spirilla is imperative to the arrest of its progress before damage is irreparable. Every recent genital ulceration should be treated prophylactically to prevent the possibility of invasion by fusospirillosis. The presence of fusiform bacilli or spirilla should not be considered primary until every effort has been made to eliminate them as secondary invaders.

The authors recommend in the treatment of these lesions a mixture of 6 Gm. of neoarsphenamine in 30 cc. each of glycerin and cod liver oil.

REUTER, Milwaukee.

PSYCHOGENIC ASPECTS OF SKIN DISEASES. JOSEPH V. KLAUDER, J. Nerv. & Ment. Dis. **84**:249 (Sept.) 1936.

One is more conscious of the skin than of any other organ, partly because it is the site of many sensations. Moreover, much concern is devoted to the beauty of the skin, and feelings of inferiority are found often in persons with even slight cutaneous lesions. On the other hand, decorations of the skin, such as tattooing and the scars of German students are often acquired with pride. Conversely, the psyche has a great influence on the skin, since all varieties of cutaneous lesions have been reported after suggestion. Thus, frights are said to have produced ecchymosis, Raynaud's disease, urticaria and other lesions. Profound cutaneous anesthesia can be induced in some persons, such as the woman reported by Strümpell who could pick eggs out of boiling water without showing burns. Klauder and Brown have demonstrated that the reactivity of the skin is decreased in animals in a state of narcosis, and this is shown in man by the absence of itching and pruritus during sleep. Klauder does not agree, however, with the opinion of some authors that herpes zoster and psoriasis may have a psychogenic basis. Erythema and blushing, on the other hand, are often associated with psychic embarrassment, and Klauder believes that angioneurotic edema, urticaria and dermatitis or eczema are manifestations of unstable action of the sympathetic nervous system. In the article several cases are briefly reported—one that of a woman who had itching of the body each Tuesday and Wednesday night. Her husband had died on a Wednesday night, having been moribund for twenty-four hours before. The psychoanalytic theory of a sexual or lustful element in pruritus—that the condition may be analogous to a masochistic act—has been overstressed, Klauder states. A considerable percentage of patients with pruritus vulvae or pruritus ani are psychoneurotic, such as the painter who exprienced pruritus ani each time he made a public exhibition of his paintings. Menninger regarded many of the excoriations of neurotic patients as masochistically attenuated forms of suicide, in that the death instinct is thwarted of its purpose through the sacrifice of a part for the whole. He stated that dermatitis factitia is a self-mutilative type of malingering, which serves as an externally directed aggression of deceit, robbery and false appeal simultaneously. Alopecia areata and sudden whitening of the hair have been traced to severe fright.

Klauder concludes that it is incumbent on the dermatologist to envisage the patient as a living personality; attention should be given to circumstances associated with the onset of symptoms and with the environmental conditions in which the patient lives.

HART, New York. [ARCH. NEUROL. & PSYCHIAT.]

ERYTHEMA NODOSUM IN CHILDHOOD. MATHILDE DE BIEHLER, Arch. de méd. d. enf. **39**:817 (Dec.) 1936.

Several theories exist concerning the origin and nature of this disease: It is regarded by some clinicians (Ferrand, Jochman and Bergman) as a manifestation of rheumatism; others (Comby and Achard) consider it an independent infectious exanthematous disease capable of mobilizing tubercle bacilli, as is found in whooping cough and measles, while another group (Arloing, Cibils Aguirre, Dufour, Landouzy and Paisseau) declares that erythema nodosum is of direct tuberculous origin.

A constantly growing number of observers seem to reconcile the disorder with anaphylactic phenomena in the course of various diseases.

Since the reports of Cibils Aguirre and Arena, who demonstrated the myobacterium in the nodules, the theory of the tuberculous nature of these nodules has been widely accepted. Primary and secondary types are described. The author has made observations in 106 cases in the children's infirmary at the University of Warsaw, the patients ranging in age from 6 months to 15 years. Seventy-four per cent of these subjects gave a positive reaction to the tuberculin test; many had suffered antecedent invasions of measles, whooping cough or influenza. Several case histories are included in the report. The conclusions drawn from this extended study include:

1. The development of tuberculosis in the course of erythema nodosum is not as common as some authors assert; in only 2 of the cases referred to was the erythema followed by generalized infection.
2. The immediate prognosis is good; there were 2 deaths among the 106 children under observation.
3. Erythema nodosum may develop in the course of any infectious disease.
4. It has been demonstrated conclusively that the disease is communicable.
5. It is encountered most frequently at the beginning of the winter and of the summer.
6. The disorder affects girls more often than boys.
7. While usually attacking the limbs, the nodules may appear on the face.
8. It is not as rare in patients of less than 5 years as is commonly believed.

AMESSE, Denver. [AM. J. DIS. CHILD.]

THE GEOGRAPHIC DISTRIBUTION OF INFANTILE ACRODYNIA. M. PÉHU, J. BOUCOMONT and LÉPANOFF, Rev. franç. de pédiat. **12**:589, 1936.

Complete information as to the geographic distribution of acrodynia is not obtainable, but from personal communications and a review of the literature the authors have found that most of the known cases occurred in France, Switzerland, Holland, Great Britain, Belgium, Germany, Australia and the United States. The Balkan peninsula, Italy and Greece have had relatively few cases, and the condition has been rare in the Scandinavian countries. The cases occur, as a rule, sporadically and in proportion to the population, they are less frequent in large cities than in small towns and rural areas. From this study it seems certain that the condition does not occur in epidemic or pandemic forms.

LESLIE, Evanston, Ill. [AM. J. DIS. CHILD.]

CONSTANT BACTERIAL FLORA IN CHILDREN'S HAIR. M. BIEHLER, Pedjatrja polska **16**:325 (Sept.-Oct.) 1936.

The work along this line is still meager. According to Hofman, investigation of the hair and the nails shows that they possess bactericidal properties of an esophylactic character. Biehler investigated 100 samples of hair, 400 investigations being made. The hairs were placed in different mediums at room temperature and at incubator temperature. There was more bacterial growth at room temperature than at incubator temperature.

The bacterium most frequently encountered at room temperature was Staphylococcus aureus, in 31 per cent; in the incubator it was present in 17 per cent. Other bacteria were seen occasionally. Yellow hair does not harbor any more bacteria than other types of hair. Bacteria were found in washed hair as well as in unwashed hair.

KRUPINSKI, Chicago. [AM. J. DIS. CHILD.]

ACTIVATION OF THE SPECIFIC TREATMENT OF SYPHILIS BY THE SUBCUTANEOUS INSUFFLATION OF OXYGEN: A PRELIMINARY COMMUNICATION. M. A. ROSENTUL, A. D. BOGODAROV, M. M. PLOTKINA and A. M. KHALETZKAYA, Vrach. delo **19**:1037, 1936.

Subcutaneous introduction of oxygen is known to have a marked influence on the vital processes, leading to increase in their activity as well as to neutralization and quicker elimination of the toxic products of metabolism. On the basis of these observations, Professor Rosentul introduced subcutaneous insufflation of oxygen as an auxiliary method for the treatment of syphilis. Experimentally it was revealed that subcutaneous introduction of oxygen makes rabbits more tolerant to the action of neoarsphenamine, an effect which the authors believe due to an increase in the oxidative processes of the body, leading in turn to more rapid and complete oxidation of neoarsphenamine and its products.

The combined neoarsphenamine-bismuth-oxygen treatment was used in 140 patients suffering from recent syphilitic infection. The patients were given from twenty to twenty-five insufflations of oxygen (doses of from 300 to 400 cc.) forty or sixty minutes before or after the introduction of the drug, an insufflation being made on the average every second day. The time necessary for the complete disappearance of the spirochetes from the lesions was compared with that necessary in the controls. The favorable therapeutic results obtained led the authors to conclude that this is the method of choice in the treatment of early syphilis, particularly if the patients are debilitated or if their tolerance of neoarsphenamine alone is poor.

BODER, Los Angeles. [AM. J. DIS. CHILD.]

TWO CASES OF MELANOSARCOMA RESULTING FROM A CALLUS. Z. NOGATA, Hihu-to-Hitunyo **4**:694 (Dec.) 1934.

Melanosarcoma in two middle-aged men, arising in each case from treating a callus on the heel, is reported as supplementary to not more than five cases of melanosarcoma with metastasis to the skin found in the Japanese literature. In both cases after the paring away of the hardened cornlike center a tendency to brownish black pigmentation developed and then rapid growth and proliferation with metastases to the regional lymph glands, the internal organs and the skin appeared. In the second case, in addition, irregular patches of depigmentation developed over the largest of the metastases (photographs), and there was intussusception due to a polypus-like metastasis in the small intestine.

BRENNAN, Chicago.

ON THE SERUM LIPOID IN EXPERIMENTAL RABBIT SYPHILIS. M. NAKANISHI, Jap. J. Dermat. & Urol. **40**:215 (Dec.) 1936.

The author found that the cholesterol content of the blood serum in syphilitic rabbits increased with the development of the clinical syphilitic changes, decreased at their height and increased gradually again during the period of their decline. These observations were made on 50 per cent of the investigated animals. In 33 per cent of the rabbits the cholesterol content reached its maximum at the height of the clinical manifestations and decreased during their decline.

The fatty acids diminished in 75 per cent of syphilitic rabbits during the phase of the strongly positive serologic reaction. An increase was noted soon after inoculation and later, during resorption of the chancre. In 25 per cent of the rabbits the fatty acids increased with the development of the syphilitic changes and reached a maximum in the seropositive phase.

Phosphatides increased in 50 per cent of the rabbits before the development and during the resorption of the chancre and diminished in the seropositive phase.

In most cases all the fractions of serum lipoids showed almost parallel variations.

The author expresses the belief that there is no close connection between the variation of the lipoid content in the serum and the Wassermann reaction.

EXPERIMENTAL INOCULATION OF LYMPHOGRANULOMA INGUINALE IN THE CAT. K. YAMAMOTO, Jap. J. Dermat. & Urol. **40**:227 (Dec.) 1936.

Young cats were inoculated intracerebrally with 1 cc. of a 10 per cent solution of material from lymphogranuloma venereum in physiologic solution of sodium chloride. Inoculation of material from human beings, which is highly virulent for mice, did not produce any clinical symptoms or specific changes, but inoculation of material from mice which had passed the mouse brain several times produced uncharacteristic clinical symptoms and specific histologic encephalomeningitic changes. The antigen prepared from the brains of the cats produced a positive Frei reaction. The transmission could be continued only to the second generation. The author concludes that the cat is not a fit animal for experimentation on lymphogranuloma venereum, thus confirming the observations of Levaditi and his co-workers.

ICHTHYOSIS AND ICHTHYOSIS-LIKE DISEASES: II. REPORT OF A CASE OF ERYTHRODERMA CONGENITALE ICHTHYOSIFORME (BROCQ). Y. KURIHARA, Acta dermat. **27**:108 (Dec.) 1936.

The author describes a typical case of erythroderma congenitale ichthyosiforme (Brocq) in a 10 year old boy who had symptoms resembling the Adams-Stokes complex, such as bradycardia, paroxysmal paleness of the face, a feeling of illness when mentally excited and periods of stuttering. According to the author, the erythema in this disease is mostly labile and indistinct and not an important symptom, and the clinical picture does not differ essentially from that of ichthyosis congenita. Erythroderma congenitale ichthyosiforme is a certain form of ichthyosis congenita characterized by erythema. The author does not agree with those investigators who maintain that keratoma palmare et plantare hereditarium or naevus keratoticus are localized forms of erythroderma congenitale ichthyosiforme (Brocq).

BLOOM, New York.

PROBLEM OF HERPES ZOSTER. S. A. GLAUBERSOHN and S. E. TRACHTENBERG, Acta pædiat. **19**:209, 1936.

Two cases are reported. In the first, exposure of a susceptible person to chickenpox led to an attack of herpes zoster; in the second, exposure to zoster produced varicella.

The etiologic connnection between herpes zoster and varicella was first suggested by Bokay, of Budapest, in 1888; in 1928 Bokay was able to collect 200 cases which illustrated this relationship, some from the literature and some from his personal experience. Despite the large number of clinical and experimental observations, the fundamental biologic relations between herpes zoster and varicella remain unsolved.

This paper contains an extensive discussion of the conflicting clinical and experimental observations relating to the perennial controversy. The opinion is expressed that a conclusive answer will not be obtained until the cause or respective causes of the two infections are identified and studied experimentally. Glaubersohn has recently had some success in preserving the virus of herpes zoster in tissue cultures. This opens the way for further investigation of the virus and for the possible use of tissue cultures in the preparation of antigens for complement fixation tests; up to the present time the use of such cultures has not been satisfactory.

MCCUNE, New York. [AM. J. DIS. CHILD.]

Society Transactions

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

JOHN E. RAUSCHKOLB, M.D., *President*

Cleveland, Dec. 5, 1936

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

A Case for Diagnosis. Presented by DR. H. G. MISKJIAN, Cleveland.

J. K., a man aged 40, is well developed and well nourished and in apparently good health. He has been suffering from his present slightly pruriginous cutaneous disease for about twenty years. The onset apparently was gradual, and the eruption has never entirely disappeared. It does not appear to be subject to any seasonal variation or other influence. There has been no ingestion of drugs.

Scattered over the body, including the palms and the soles and excepting the face, there is a nodular eruption of rather remarkable symmetry. The total number of lesions approximates a hundred. In some places there is definite herpetiform grouping, and the lesions are in various stages of development. The lesions begin as small sharply defined red areas, gradually become raised above the level of the skin, and develop into rather hemispherical nodules whose average size is that of a split pea. Later they become covered with white or yellowish white scales or crusts. Removal of these crusts reveals a superficial moist erosion. There is no pus. The older lesions become flattened, undergo progressive regression and disappear, leaving a brownish red macule with evidence of slight atrophy. The entire cycle of development and regression takes from three to four weeks. There is a macerated type of dermatophytosis between the toes. Studies of the blood, including serologic examinations, showed no abnormality.

A specimen taken for biopsy showed slight spongiosis in the epidermis, especially in its deeper portions. There was some edema in the papillary layer of the corium. A number of dilated blood vessels were found in the subpapillary layer. They were surrounded by a moderate cellular infiltration around the hair follicles and contained a number of polymorphonuclears and eosinophils, along with numerous lymphocytes, but the bulk was composed of cells belonging to the reticuloendothelial system.

The patient has had a great many treatments with roentgen rays. I have convinced myself of the inefficiency of this method by treating individual lesions and observing them closely. Arsenic has been given by mouth.

DISCUSSION

DR. HARTHER L. KEIM, Detroit: I believe this case is an example of lymphoblastoma of the mycosis fungoides type. The chronicity, the pruritus and the character of the lesions speak especially in favor of this type of process. Lesions which are simple desquamating infiltrates are to be found, and there are nodules of various sizes, some of which tend to ulcerate. The mild increase in circulating lymphocytes is likewise suggestive.

DR. BENJAMIN LEVINE, Cleveland: The patient states that at one time, after he had taken iodized salt, an acneform eruption appeared. When closely questioned he says he does not take iodine or any other medication, but has been in the habit of eating sea food once a week. It is possible that in this way he could ingest a small amount of iodine, which could possibly keep up the activity of the lesions.

DR. SAMUEL GOLDBLATT, Cincinnati: On questioning the patient, I discovered that he has been a dictaphone operator for twenty years, and began his work just before the eruption occurred. He never worked at any other occupation and has never been tested for sensitivity to any of the products associated with dictaphone work. I suggest that this be done.

DR. LESTER HOLLANDER, Pittsburgh: My impression is that the patient has marked ichthyosis which has been present since birth. Superimposed on it is a nodular eruption which first began about twenty years ago. Some of the nodular lesions present evidence of central necrosis. These lesions are painful and tender. Unless they are traumatized they disappear without scar formation. In the main, they have many characteristics of papulonecrotic granuloma, suggesting a systemic follicular eruption.

DR. H. G. MISKJIAN, Cleveland: I am thankful for the suggestions made. In regard to the diagnosis of lymphoblastoma, including mycosis fungoides, let me say that this man has had his eruption for twenty years. I think the duration of the disease is sufficient to rule out that possibility. The histologic picture was against that diagnosis. It showed a peculiar dense, sharply defined infiltration around a hair. This infiltration contained many polymorphonuclears and eosinophils but was composed mainly of cells with rather abundant clear protoplasm. These cells, so far as I could make out, belonged to the reticulo-endothelial system. Dr. David L. Satenstein, of New York, to whom I sent the slide, called my attention to the fact that this type of infiltration is seen in iodide eruptions. The patient says that he does not take iodized salt or any medicine. In regard to the suggestion of dictaphone dermatitis, I shall be glad to investigate, but it seems to me that the eruption is not of the type one would usually find in allergy. Tuberculin tests were not made because the lesions were not those of any form of cutaneous tuberculosis, and the histologic picture seemed to rule out that disease. The elements are papules and nodules, but none of them show the central necrosis characteristic of papulonecrotic tuberculid.

Pseudoxanthoma Elasticum with Angioid Streaks of the Retina. Presented by DR. EDWARD HENRY JONES, Youngstown, Ohio.

E. F., a housewife aged 44, has always enjoyed good health, with the exception of a severe attack of measles at the age of 1½ years. The present eruption started in 1925 and has never produced any subjective symptoms. The lesions are numerous, involving the neck, the trunk and the thighs, and consist of variously sized and irregularly shaped plaques and patches of a somewhat yellowish color. Many of the lesions are firm and indurated and seem scarlike to palpation. In some instances there is atrophy, and in some instances the plaques assume a linear arrangement and the color varies from chamois yellow to orange.

Examination of the eyegrounds showed partly blanched streaks paralleled by pigment, located deep in the retina and faintly resembling closed blood vessels. Studies of the blood, including serologic tests and Mantoux tests, showed no abnormality. Roentgenograms of the chest showed nothing abnormal.

Treatment, consisting of roentgen and ultraviolet irradiation and injection of nonspecific proteins, has been without effect.

DISCUSSION

DR. LESTER HOLLANDER, Pittsburgh: For the diffuse infiltrating lesions I want to offer the diagnosis of nodular tuberculosis of the hypoderm, described by Wende.

DR. R. E. BARNEY, Cleveland: I do not know whether all the members have noticed the lesions on the legs. I do not think sufficient emphasis has been placed on them. These nodules were rather deeply seated and suggested sarcoid.

DR. UDO J. WILE, Ann Arbor, Mich.: A large number of giant cells were entirely independent of tuberculoid reactions. They were a foreign body type of giant cell.

DR. E. W. NETHERTON, Cleveland: I should like to emphasize the fact that those who have discussed this case failed to make any remarks regarding the yellowish plaques along the axillary margins and along the anterior portion of the chest. These have been thought to be pseudoxanthoma elasticum, and I understand that this patient has angioid streaks in the left retina. Dr. Jones has taken a biopsy specimen from one of the cutaneous lesions but was unable to get a section before the meeting.

Lupus Erythematosus; Lichen scrofulosorum. Presented by DR. H. N. COLE and DR. J. R. DRIVER, Cleveland.

R. H., a man aged 31, had been in excellent health until the spring of 1936, when he had a sore throat associated with intestinal influenza. After this his temperature was elevated for several weeks. That manifestation disappeared, but pains persisted in his abdomen, and he had night sweats. About May 1936 pain developed in the foot and other joints, and about six weeks later he noticed an eruption on the skin behind the ears and later on other parts of the body. He consulted several physicians and visited several clinics.

There is an eruption over the extensor surfaces and the face. On the face the lesions are roughly round, slightly indurated, dark pink patches, with some crusting, one being on the nose, one on the forehead and one on the cheek. Over the body the lesions are follicular and made up of papules and pustules. In places these plaques have a tendency to run together. There is no annular configuration associated with the lesions. The tonsils are somewhat injected. The lungs are clear. The cardiovascular stripe shows nothing abnormal. Examination of the abdomen showed nothing abnormal. Both hands and the fingers are swollen. The knee is swollen, tender and partially fixed. There is no edema of the ankles. The blood pressure is 118 systolic and 70 diastolic. Blood counts, blood cultures and serologic tests showed no abnormality. Gastric analysis gave normal results. Intradermal tuberculin tests gave negative results with all dilutions down to 1:10. The basal metabolic rate was +3 per cent. Roentgenograms of the gastrointestinal tract showed a picture consistent with duodenal ulcer. Roentgenograms of the chest showed no abnormality. A specimen taken for biopsy from a lesion on the arm showed multiple inflammatory lesions scattered throughout the corium and in association with the hair follicles and the sebaceous and sudoriferous glands. These were characterized by central caseous necrosis, and there was a delimiting zone of epithelioid cells, typical Langhans' giant cells and surrounding lymphocytic infiltration.

Histologic examination of a lesion on the back showed the epithelium to be thinner there than in a section from the lesion on the arm. There were less tendency to central necrosis, less well developed epithelioid cells and greater variation in types of giant cells. Many were small and resembled the foreign body type. The patient was directed to rest in bed, and boric acid ointment was applied locally. The condition improved a great deal.

DISCUSSION

DR. LOREN W. SHAFFER, Detroit: The occurrence of lichen scrofulosus in association with lupus erythematosus is one of the points taken to prove the tuberculous etiology of lupus erythematosus. Cases in which such an association occurs should, therefore, be examined carefully. From what I can see clinically, there is no definite evidence of lupus erythematosus in this case at present. A few scattered lesions on the face are more suggestive of tuberculosis cutis. I therefore think the whole picture can be more properly assigned to a place among conditions of strictly tuberculous etiology.

DR. R. E. BARNEY, Cleveland: I agree with Dr. Shaffer. I could not make a diagnosis of lupus erythematosus. I do agree, nevertheless, with a diagnosis of lichen scrofulosus. In addition, I should like to call attention to the nodules on

the forearms and to one nodule, especially, between the left thumb and the index finger. I should like to put these lesions in the same category and interpret the nodules as sarcoid.

DR. G. W. BINKLEY, Cleveland: I think this case is interesting from the standpoint that in this country there are so many cases of lupus erythematosus in which there are no tuberculous foci. The man did have characteristic lupus erythematosus, and this condition has faded out, leaving a picture of lichen scrofulosus. He shows an unusual combination of lupus erythematosus and lichen scrofulosus with tuberculosis at the background. I have seen many cases of lupus erythematosus, but none presented tuberculous lesions.

DR. H. N. COLE, Cleveland: This patient has not been seen since July. At that time he had characteristic butterfly lesions suggestive of lupus erythematosus. There are still some to be seen today. He undoubtedly has lupus erythematosus as well as lichen scrofulosus. In regard to the nodules on the elbows and the face and the others on the body, I understand the patient has had them for several years. I am not sure how long. Tuberculosis is assumed to be in the background of the picture.

Dermatofibrosarcoma Protuberans. Presented by DR. MAURICE SULLIVAN, Cleveland.

E. D., a man aged 32, from the service of Drs. H. N. Cole and J. R. Driver at the Lakeside Hospital, has had acne vulgaris since 1920. A year and a half ago the patient first noticed a lump on his back, which grew to the size of a walnut. A second mass grew on top of the first one. He reports that three or four weeks ago these masses discharged a clear fluid but stopped after several days. Two weeks ago the lesion became painful and sore, with frequent shooting pains radiating through the left side of the chest. These pains were transient but were accompanied by dizziness and weakness.

At the level of the tenth rib posteriorly, about 3 inches (7.5 cm.) from the midline on the left side of the chest, is a purple-red oval mass measuring 7 by 4 cm., whose long diameter is directed downward and to the left. The mass consists of two parts: one, occupying the lateral third of the tumor, is like a walnut that projects above the level of the remaining part; the other, making up the medial two thirds, is less raised. On palpation one finds that the tumor extends farther out under the skin than the area of redness would indicate. It is adherent to the skin in the center, where the color is red, but is freely movable on the deeper layers. The projecting portion is much firmer than the medial flatter portion. The latter when palpated gives a feeling of false fluctuation. The face and the back are covered with numerous acneform lesions. The blood pressure was 142 systolic and 80 diastolic. Physical examination and serologic tests showed no other abnormality.

Histologic examination showed the tumor to be made up of poorly defined narrow streams of elongated cells with scanty attenuated acidophilic cytoplasm and relatively large long slender nuclei, which characteristically had flattened ends. There was moderate variation in the size and the shape of the nuclei. In places there was a tendency for the nuclei of contiguous cells to have a palisade formation. The tumor was moderately well vascularized, and the blood vessels had intact walls. There was little collagen.

DISCUSSION

DR. G. S. WILLIAMSON, Ottawa, Canada: Clinically and histologically this lesion resembles those described by Darier under the name *dermatofibromes progressifs et récidivants (Ann. de dermat. et syph.* **5**:545, 1924). These lesions lack the characteristics of true sarcoma, as they do not cause adenopathies, and internal metastases are unknown.

DR. I. J. ARNSSON, Buffalo: The pathologic specimen does not show any malignancy. I believe the condition is plainly fibroma.

DR. R. E. BARNEY, Cleveland: In addition to the lesion described, the man presents another interesting condition, involving the back especially and characterized by so-called bridge scars, many of which present comedones suggesting a diagnosis of acne conglobata.

DR. M. W. RUBENSTEIN, Pittsburgh: I agree with the diagnosis as presented, and I believe the condition is malignant. The character of the cells speaks for a a malignant process rather than a benign one. I should like to ask the presenters why the section was taken from the central portion of the lesion instead of the periphery. In sections taken from the periphery, one sees more definitely the character of the growth particularly and the presence or the absence of a capsule, and the extent of the lesion can more or less be determined.

DR. H. J. PARKHURST, Toledo, Ohio: I agree with the diagnosis. An interesting point to be considered is whether or not this eruption may have arisen from acne.

DR. H. N. COLE, Cleveland: This patient was seen only a few days ago. The picture is rather unusual, and when palpated the process has an almost cystic feel at the base, which makes difficult an association with dermatofibrosarcoma of Darier. I have therefore considered the possibility that the condition is acne with keloidal development. The section was sent to the pathologist, who diagnosed the condition as neurofibromatosis, but of course the general pathologist has no knowledge of this condition, originally described by Darier. The process always comes back, and the patient usually dies. Therefore, it is a malignant disease.

Lupus Erythematosus with Unusual Oral Lesions. Presented by DR. H. N. COLE and DR. J. R. DRIVER, Cleveland.

T. B. a man aged 31, appears to be well developed and well nourished. For nine years he has had spots on his eyebrows, above the eyes and in front of the ears. For seven years the prepuce has been involved, and circumcision was performed. Tonsillectomy was performed in 1935, but there was no improvement in the condition of the skin.

Located symmetrically on the face are many chronic lesions, irregular, reticulated and patchy, with considerable adherent scaling. The eyes are suffused and injected, both the palpebral and the occular conjunctiva being involved. The vermilion border of the lower lip shows a scaly erythematous change, and the palate presents several eroded papules the size of a split pea. Involvement of the glans penis in the region of the meatus has produced some scaling and stenosis. The under-surface of the shaft of the penis is involved.

Studies of the blood and serologic tests showed nothing abnormal.

A specimen taken from the palate for histologic examination showed spongiosis and acanthosis of the epithelium. There was edema in the superficial layer of the corium and marked congestion of the blood vessels. Throughout the corium there was a dense infiltrate consisting of lymphocytes, plasma cells and, in the deeper layers, a few fixed connective tissue cells.

A section from the skin showed slight parakeratosis. The epidermis was thinned. The interpapillary pegs were absent. Horny plugs filled the dilated ostia. In the superficial layer of the corium there was peculiar degeneration of the connective tissue. Edema and perivascular, as well as perifollicular and diffuse lymphocytic, infiltration characterized the remainder of the corium. Treatment has consisted of a course of ten intramuscular injections of bismuth and potassium tartrate, 0.13 Gm. each, and iodoform and mass of ferrous carbonate pills internally. Recently the patient has been receiving injections of gold sodium thiosulfate, the doses ranging from 10 to 25 mg. There has been moderate improvement.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: The microscopic picture is unusual for lupus erythematosus. Some of the lesions are yellowish, and I wonder if the

presenters considered the possibility that the condition might be an unusual form of lupus vulgaris erythematoides.

DR. STANLEY CRAWFORD, Pittsburgh: I agree with Dr. Wile that the facial involvement is suggestive of lupus vulgaris erythematoides of Leloir. The diascope reveals many minute superficial lupous nodules with typical apple jelly color, and the microscopic section, showing many plasma and giant cells, rather supports this diagnosis. The combination of lupus vulgaris of the face and lupus erythematosus of the hard palate and the glans occurs rarely.

Pigmented Basal Cell Epithelioma, Showing Residual Pigmentation After Treatment. Presented by DR. E. W. NETHERTON, Erie, Pa.

M. D., a man aged 49, states that there has never been any cancer, tuberculosis or other chronic illness in his family. About ten years ago a small dark crusted lesion appeared on the right side of the nose. When the crust separated, a small black nodule remained. This pigmented lesion gradually enlarged by peripheral extension. The advancing margins remained pigmented and have always been preceded by a narrow zone of bluish black pigmentation. Although the margins remained hyperpigmented, the central portion of the lesion became a depigmented, atrophic scar; however, the original nodule remained, and the skin directly over it remained slightly hyperpigmented.

On July 3, 1935, there was a large serpiginous, sharply defined noninflammatory lesion involving most of the right side of the nose and the adjacent areas of the cheek. It extended from near the inner canthus along the bridge of the nose and involved the ala of the right nostril. The margins of the lesion were raised, rolled and bluish black, and in places there were loosely adherent black crusts. The base bled easily when the crust was removed. The central portion consisted of a depigmented atrophic scar. There was a freely movable slightly pigmented cutaneous nodule the size of a split pea at the site of the original dark crust. There were many comedones at the periphery of the lesion. There were no subjective symptoms. At present the margins are somewhat hyperpigmented, but the neoplastic condition has disappeared.

The Wassermann and the Kahn test of the blood were negative, and other serologic studies showed no abnormality.

A specimen taken from the ala of the right nostril for histologic study showed almost complete loss of surface epithelium and, extending from the surface of the lesion downward into the corium, solid irregular strands or masses of spindle-shaped epithelial cells. There was no pearl formation. There were many large cells in the stroma which contained melanin. There were melanin-containing cells within the masses of epithelial cells. There was a moderate amount of lymphocytic infiltration deep in the corium. The pigment-containing cells stained black with silver nitrate, and there were dopa-positive cells in the basal layer of the epidermis and in the papillary layer near the epithelial downgrowths.

The patient has been treated with radium with good results. At present there is questionable recurrence in one or two areas.

DISCUSSION

DR. S. W. BECKER, Chicago: Basal cell carcinoma is pigmented because there are normal melanoblasts associated with carcinomatous cells. As Dr. Netherton stated, most of the pigmentation one sees on examination of the section is in chromatophores. It is a known fact that pigmentation by chromatophores may remain for a good many years. I have a section from a case in which melanin was injected into a vitiliginous area. After eight years one can still see many chromatophores. This pigmentation slowly fades out over a period of years, as from a tattoo.

DR. E. W. NETHERTON, Cleveland: The case is presented because of the marked amount of pigment present. I am glad to hear of Dr. Becker's experience.

Boeck's Disease (Generalized Sarcoid). Presented by Dr. G. W. Binkley, Cleveland.

M. A., a Hungarian woman, aged 48, from the service of Drs. H. N. Cole and J. R. Driver at the City Hospital, dates her complaint from February 1935, at which time there were pain and swelling in the joints of the hands and the feet. In October of the same year she was admitted to the City Hospital, where a diagnosis of chronic inflammatory arthritis and allergic rhinitis was made. She was given six fever treatments with the Kettering hypertherm, which produced considerable relief from pain. During her stay in the hospital several nodules developed in the skin. These increased in number and the symptoms in the joints recurred within the next few weeks. Between January and July 1936 roentgen therapy was administered to the cutaneous lesions, and partial regression ensued. The patient left the hospital and was readmitted on Nov. 28, 1936, at which time she had become greatly emaciated. The lesions in the skin had become more numerous, and there was a tumor present on the nasal mucosa. The tonsils were large. All the superficial lymph nodes were moderately enlarged. There were hydrothorax on the left side, ascites and general anasarca. The liver was percussed 3 fingerbreadths below the costal margin. There was fusiform swelling of the phalanges. The cutaneous lesions consisted of sharply defined firm dull red nodules and tumors, ranging from 0.5 to 2 cm. in diameter. Roentgenograms of the bones of the hands showed demineralization and destruction of the terminal phalanges in several instances. Roentgenograms of the pelvis, the skull and the feet showed no abnormality.

Numerous blood counts were made, the number of red cells ranging from 4,200,000 at the start progressively to 2,000,000. The white cell count averaged between 4,000 and 5,000. The hemoglobin was progressively reduced from 90 to 38 per cent. Differential blood counts showed considerable variability, but there were usually about 65 per cent polymorphonuclear cells. The number of small and large lymphocytes ranged between 17 and 43 per cent. Monocytes were present in as high a proportion as 10 per cent in one count. The eosinophil count ranged from 2 to 12 per cent. The urea nitrogen and cholesterol contents of the blood were within normal limits; the uric acid content ranged from 3.6 to 4.9 mg., and the calcium content was 13.8 mg. per hundred cubic centimeters. Examination of the urine revealed occasional traces of albumin. Mantoux tests gave negative results with dilutions down to 1:10. The Wassermann test of the blood was negative.

Histologic examination of one of the cutaneous nodules showed a flattened epidermis. Throughout the corium at all depths were many sharply defined nodules of an infiltrate separated by connective tissue septums. These nests were made up of epithelioid and connective tissue cells, and under high power magnification frequent mitotic figures could be seen.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: I dissent from the diagnosis. It seems to me that both microscopically and clinically the picture shows a malignant condition not unlike that of melanoblastoma. I cannot see anything like sarcoid in the clinical picture or in the microscopic slide.

Dr. Lester Hollander, Pittsburgh: I support the diagnosis of sarcoid of Boeck in this case. The clinical picture is similar in a good many respects to that in a case an associate and I reported (Hollander, L., and Schlesinger, C. R.: Sarcoid of Boeck, Arch. Dermat. & Syph. **29**:387 [March] 1934). I think the roentgenologic evidence is conclusive. Many of the phalanges show cystic osteitis, which Kissmeyer, of Copenhagen, Denmark, considers an important part of the clinical picture. In addition to the massive exudate involving the left lobe of the lung, the roentgenograms show diffuse infiltration at the hilus. It is true that this patient looks cachectic, and a diagnosis of extensive sarcomatosis should be

taken into consideration. With the amount of involvement which she presents, sarcoid of Boeck can produce this amount of cachexia.

DR. CLYDE K. HASLEY, Detroit: I wish to support the diagnosis of Boeck's sarcoid, because the roentgenograms show a destructive bony involvement typical of this disease. It is a known fact that Boeck's sarcoid frequently presents destructive bony involvement, even months before the lesions of the skin appear.

DR. HOWARD T. PHILLIPS, Wheeling, W. Va.: I agree with Dr. Wile. I believe the development of the process has been entirely too rapid for sarcoid. To me the condition appears to be generalized sarcomatosis. The extreme cachexia and the rapid loss of weight help to substantiate this diagnosis.

DR. JOHN WILLIAM JORDAN, Chicago: I agree with the diagnosis of Boeck's disease or generalized sarcoid, as presented. I recently had the occasion to observe two similar cases. One was that of a Negro child, who had all the manifestations that this patient presents and who subsequently died of pulmonary tuberculosis; the other, that of an adult, who has had the condition for approximately ten years and is alive and otherwise well.

DR. UDO J. WILE, Ann Arbor, Mich.: What would explain the amount of mitosis seen here unless the condition were malignant? Practically every cell is dividing.

DR. H. N. COLE, Cleveland: I am much interested in Dr. Wile's suggestions. My associates and I shall follow this patient and see what develops. We shall try to keep reports in the scientific literature up to date. There are typical digital lesions here. The lesions, if one examines them histologically, show characteristic infiltrated areas, separated by fibrous septums. The lesions are hard nodules, with variations in size and color such as one would expect in sarcoid. I remember in the private practice of Dr. J. R. Driver and me one patient in whom fifty or sixty nodules developed in six months. I think the rapidity of development is not against sarcoid.

SUBSEQUENT NOTE.—On Jan. 2, 1937, the patient died. Autopsy was performed, and a pathologic diagnosis of aleukemic reticulo-endotheliosis with clinical features of generalized sarcoid was made.

Acrosclerosis. Presented by DR. G. W. BINKLEY, Cleveland.

D. M., a woman aged 41, from the service of Drs. H. N. Cole and J. R. Driver at the City Hospital, had always been in good health until ten years ago, when pain developed in the fingers. The condition was aggravated when the patient was exposed to cold, at which time the fingers became cyanotic. The disease has been progressive, involving the face at the same time in a scleroderma-like condition. The terminal phalanges of the left four fingers have gradually atrophied and eventually have been destroyed. At present the face is masklike; the skin is somewhat thickened and rubbery, and on its surface there are some reddish macules with telangiectasia. There are firm macular lesions on the forearms and some associated brownish pigmentation. The fingers present symmetrically healed stumps.

Serologic tests for syphilis gave negative results and routine examination of the blood showed no abnormalities.

Histologic examination showed some hyperkeratosis. The epidermis was narrow, and there was budding similar to that in acanthosis. The interpapillary pegs were avascular and stained dark red with eosin. No small blood vessels were found, but deep in the corium were a few large thick-walled vessels with narrow lumens. The sweat glands were prominent and were located near the surface. Collagen stains showed dense intertwining bundles of connective tissue.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: This case is worth discussing, on account of two or three unusual clinical features. In the first place, the patient has on the face and the hands interesting telangiectatic lesions such as might have been

caused by irradiation. Then, the acrosclerosis is not associated with acro-asphyxia, and there was no evidence of pre-existing Raynaud's syndrome. This form of deformity could be explained on the basis of some central disturbance. One might think of leprosy. I tested this patient rather hastily with a pin, and while nothing definite was noticeable, there were areas of lessened perception of pain and touch, as compared to others. Definitely there was some evidence of anesthesia on the arms and the hands. I believe this condition is not ordinary acro-asphyxia with acrosclerosis, usually associated with a perivascular condition. The question of anesthetic leprosy should be considered in this case.

DR. S. W. BECKER, Chicago: I agree that this is an unusual condition. A patient was presented before the Dermatological Conference of the Mississippi Valley on Sept. 12, 1936 (ARCH. DERMAT. & SYPH. **35**:973 [May] 1937), with a diagnosis of telangiectasia macularis eruptiva perstans and with lesions identical with those which this patient presents. The woman was aged 31 and of Scandinavian descent. Her condition started with pallor of the hands on exposure to cold. She had had generalized pruritus for nine years but did not present sclerodermatous changes similar to those presented by the patient today. There was definite evidence of infection, in the form of ulcers on the calves. The sections from her skin did not show vascular obliteration. In both patients stroking of the lesions was followed by immediate return of blood. Ehrmann called attention to this manifestation as indicating organic obliterative vascular disease. In this patient this vascular obliteration is shown in sections. Strangely, this patient does not have the same changes in the feet as in the hands. In Raynaud's type of scleroderma the hands and the feet are uniformly involved. The picture here seems to fit in with Sellei's classification of acrosclerosis and not with Raynaud's type of scleroderma. The vascular obliterative changes suggest infection as the causative factor.

DR. G. W. BINKLEY, Cleveland: After careful study of Sellei's work on this disease I was convinced that the case would have to be labeled with this diagnosis. When I finished reading the description I felt that my patient had all the symptoms of the disease, the masklike face, the loss of the phalanges, the pigmentation in the skin, the telangiectasia and the vasomotor changes which are found when the patient goes from a warm room to a cold one. The thing I should like to stress is that this condition is acrosclerosis, which is symmetrical, and must be differentiated from scleroderma, which is asymmetrical. The conditions are different. In regard to leprosy, the patient was born in Greece but has lived in this country practically all her life. The process has come on slowly over the past ten years. I do not think it is leprosy.

CLEVELAND DERMATOLOGICAL SOCIETY

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Jan. 28, 1937

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

Gamasoidosis. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

Mrs. R. L., a woman aged 63, consulted us two weeks ago. She stated that for nine years she had endured recurrent pruritus on the neck, the wrists and the forearms. She noticed that when she left her residence in the city to live in the country during the summer the eruption and pruritus disappeared; when she returned to the city, however, there was a recurrence. She had consulted many physicians

and had had various types of treatment, none of which had given her any permanent relief. She has had a canary in her house in the city for something over nine years, and inquiry revealed that she had often noticed small reddish spots on the white cloth she used to cover the cage at night.

The eruption located on the neck, the forearms and the hands is a dermatitis consisting of grouped, diffuse scaly lesions with excoriations. On the palms and the wrists are tiny succulent papules.

Examination of feathers from the canary disclosed the presence of Dermanyssus gallinae in large numbers.

DISCUSSION

DR. MAURICE SULLIVAN, Baltimore: The finding of the avian mite D. gallinae on the feathers, the cessation of the pruritus and involution of the process after the bird and its cage had been destroyed and the appearance of the eruption—particularly the presence of little succulent papules in the areas of "dermatitis"—together justify the diagnosis. Sulzberger and Kaminstein (ARCH. DERMAT. & SYPH. **33**: 60 [Jan.] 1936) have recently reported five cases of dermatoses due to avian itch mites from pet canaries.

D. gallinae is a vampire and depends on its host for sustenance. Unlike Acarus scabiei it never burrows and cannot live long or reproduce on man. As soon as the obligatory host is removed, the mite perishes.

Livedo Reticularis (Due to Syphilis?). Presented by DR. JARRETT ARTHUR COOPER (from the Department of Dermatology and Syphilology, the Lakeside Hospital).

E. K., a white woman aged 29, presents a mottled and marbled appearance of the skin of the lower extremities produced by a network of reddish or bluish irregular lines surrounding normal skin. The appearance suggests atrophy in some areas. The hands and fingers appear cyanosed when dependent. General physical examination showed no other abnormality. The blood pressure is 138 systolic and 90 diastolic, and the basal metabolic rate, —13 per cent. The Wassermann and the Kline test were negative. In 1929 she delivered a macerated stillborn child at full term. This was the only time at which she was pregnant. Histologic examination showed low epithelium with a suggestion of atrophy. There was mild hyperkeratinization, especially at the hair follicles. The corium showed some swelling of the fibrous connective tissue. Weigert's stain showed indistinct elastic tissue fibers of normal length. There were many small blood vessels just below the epidermis. In some places they were arranged in a line. A slight cellular infiltrate was noted around some of the vessels, and there was a suggestion of thickening of the walls.

DISCUSSION

DR. H. N. COLE: In spite of negative reactions to blood tests for syphilis and of a lack of any physical indications of the disease, I believe this case is one of livedo reticularis due to syphilis. Histologic observations pointed to this diagnosis, and the pregnancy resulting in a macerated fetus is highly suggestive.

Leiomyoma Cutis. Presented by DR. C. L. CUMMER and DR. C. G. LAROCCO.

M. L., a white woman aged 56, presents on the left anterior wall of the chest a group of several lesions consisting of firm chamois-yellow pea-sized nodules which have been present for eight years. The lesions are senstive to palpation. In the region of the left shoulder there are some flat dusky red plaques showing some induration and atrophy and one lesion, approximately 2 cm. in diameter, with a rounded top, of jelly-like consistency and resembling sarcoid. The Wassermann reaction was 2 plus, and the Kline, 4 plus.

Biopsy showed the cutaneous surface to be covered with thin but regular squamous epithelioma. Extending upward to the epithelium and infiltrating irregularly into the underlying subcutaneous fat were thick bands of smooth muscle tissue disposed in parallel and interlacing bands and whorls, with much fibrous tissue. In this mass were seen isolated spaces and sudoriferous glands.

DISCUSSION

DR. H. N. COLE: The small nodular lesions clinically appear to be leiomyoma. The larger lesion in the region of the shoulder clinically is suggestive of sarcoid. The biopsy specimen, however, clears up the diagnosis without any question.

DR. E. W. NETHERTON: I should like to ask the presenters if they have any explanation of the fact that lesions of leiomyoma are so painful to palpation.

DR. C. L. CUMMER: The pathologist at the Charity Hospital who examined the section believes that there is a considerable amount of nerve tissue, which may account for the unusual amount of pain when pressure is exerted on the lesion.

Three Cases of Tuberculosis Verrucosa Cutis. Presented by DR. S. C. BOWEN (from the Department of Dermatology and Syphilology, the Lakeside Hospital).

CASE 1.—A. E., a white man aged 50, born in Austria, employed as a motor mechanic, shows on the dorsum of the right thumb a warty papillomatous and granulomatous lesion, approximately 4 by 6 cm. There is no ulceration. There is a surrounding area of erythema. The lesion has been present for about three years, increasing gradually in size. Two and one-half months ago a cold in the chest developed and there was considerable sputum. The patient states that he has been in the habit of wiping his mouth with the back of his hand.

Roentgenograms of the chest showed bilateral chronic fibroid pulmonary tuberculosis of the upper lobe of each lung. This diagnosis was confirmed by physical examination of the chest. The sputum showed tubercle bacilli. The Wassermann and the Kline test were negative.

Histologic examination of sections of the skin and subcutaneous tissue revealed marked hyperplasia, with elongation and thickening of the retes and hyperkeratosis. Many of the elongated and broadened retes were filled with keratohyalin and others with a mixture of cellular débris and exudate. There was a plaquelike thickening of the corium, represented by a syncytium of poorly outlined small polyhedral cells which in places resembled epithelioid cells. Throughout this zone occasional small multinucleated giant cells of the Langhans type could be identified. There was degeneration of the tips of some of the retes but no caseation. The tissue was sparsely infiltrated by exudative cells, including a few eosinophils.

CASE 2.—E. S., a housewife aged 61, born in England, presents on the dorum of the right wrist a verrucous, slightly elevated, crusted granulomatous lesion about 7 cm. in diameter. There is a similar lesion at the base of the ring finger of the right hand, about 1 cm. in diameter, and on the flexor surface of the right arm are two partially healed lesions of about the same size. One son has active pulmonary tuberculosis, and three other children are said to be underweight. The lesion on her wrist has been present for nine years and started after she had opened a small callous with a sewing needle. It has gradually progressed until the present time.

Roentgenograms of the chest showed extensive calcification of the region of the hilus on both sides.

The biopsy showed acanthosis and hyperkeratosis, with intra-epithelial abscesses. The entire corium was infiltrated with all types of inflammatory cells. There were areas in which these exudative cells were more dense and showed newly formed blood vessels, fibroblasts and small focal areas of eosinophils. The Ziehl-Neelsen stain failed to reveal any acid-fast bacteria in the tissue. No giant cells were noted.

CASE 3.—J. K., a man, aged 64, a carpenter, presents on the dorsum of the left hand over the first, the second and the third metacarpal an irregularly shaped

verrucous and granulomatous dirty gray lesion with some crusting. The patient states that the lesion began about three years ago as a small pea-sized wart, which was removed by cauterization in June 1935. After this the process began to spread and increased gradually to its present size, approximately 5 cm. in diameter. In 1935 the patient had pulmonary tuberculosis, and tubercle bacilli were demonstrated in the sputum.

DISCUSSION

DR. J. R. DRIVER: This group of cases furnishes an interesting illustration of the usual method of inoculation. The lesions are usually found on the hands, as in these cases. In the first one there is a history suggestive of inoculation on the hand from the mouth.

In the second case the prick of a needle which perhaps had previously been in contact with the mouth may have been the source of infection.

In most instances some type of trauma has resulted in inoculation with the tubercle bacillus. In all three of these cases there is a definite history of pulmonary tuberculosis.

DR. JOHN E. RAUSCHKOLB: I should like to suggest treatment by curettage and the application of powdered potassium permanganate in these cases. My associates and I have had good results in a few cases with this method.

DR. R. E. BARNEY: I should hesitate to treat this condition by any destructive measure which might result in liberating tubercle bacilli into the lymph channel or into the blood stream. A safer form of treatment would be radiation therapy.

Subacute Disseminate Lupus Erythematosus. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

V. T., a colored woman aged 28, complains that in March 1936 an eruption developed on her face, associated with edema of the eyes. The eruption became more extensive, involved the scalp and resulted in almost total loss of hair. The eyebrows were involved. Involvement of the arms and the forearms progressively took place, and at various intervals her condition was marked by exacerbations, associated with a moderate febrile reaction.

The patient is emaciated, weighs 96 pounds (44.5 Kg.) and presents a strikingly symmetrical eruption of the scalp, the face, the neck and the upper extremities. The eruption consists of annular and papular lesions varying in diameter from a few millimeters to 2 cm. In some of the earlier lesions vesiculation is noted. Secondary changes consist of deep pigmentation, desquamation and moderate atrophy. There is almost total loss of hair on the scalp and the eyebrows.

Roentgenographic examination of the teeth and sinuses showed no focal infections, and roentgenograms of the chest showed no evidence of active tuberculosis. The erythrocyte count remained at approximately 4,000,000. The leukocyte count fluctuated from 4,250 to 7,750. The differential count was normal.

Histologic examination showed the epidermis to be thinner than normal. There was slight hyperkeratosis but no follicular plugging. The atrophy of the epidermis was associated with flattening of the epithelial cells. The basal layer was much distorted by edema (acantholysis). In the corium there were diffuse edema, degeneration of the collagen, dilatation of the blood vessels and little infiltrate.

Medication by injections of a gold compound was discontinued after the fifth injection because of intolerance.

DISCUSSION

DR. H. N. COLE: At present the condition seems to be in partial remission, and the patient is afebrile. At various times she has had lesions in the mouth which I felt were characteristic of lupus erythematosus. In certain of the lesions on the face and the scalp there is suggestive follicular plugging. The follicular and bullous character of some of the lesions is seen sometimes in disseminate lupus erythematosus.

JOHN E. RAUSCHKOLB, M.D., *President*

Feb. 25, 1937

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

Subacute Disseminate Lupus Erythematosus. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

V. T., a Negress aged 28, was presented at the January meeting (ARCH. DERMAT. & SYPH., in this issue, p. 325) and is presented again because of developments that have taken place in the meantime. Approximately one week after having been presented at the meeting a cough developed, and there was profuse purulent sputum. Physical examination and roentgenograms of the chest confirmed a diagnosis of bronchopneumonia. Smears and cultures of the sputum revealed a pneumococcus. About two weeks after the onset of pneumonia acute inflammatory arthritis developed in the right elbow; this became greatly swollen, and aspiration and culture of purulent material from the joint showed a pneumococcus. During the febrile course of the disease the lesions of lupus erythematosus completely resolved, and the patient now presents only mildly atrophic areas where the previous lesions were.

DISCUSSION

DR. G. W. BINKLEY: My associates and I have re-presented this case in order to show the remarkable improvement that has resulted, apparently owing to the fever caused by the pneumonia.

DR. BENJAMIN LEVINE: I should like to report a similar case that I observed about three years ago in which disseminate lupus erythematosus cleared after an attack of pneumonia. The patient has remained well.

A Group of Cases of Tinea Capitis. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

Several children were presented for demonstration of fluorescence with Wood's filter. Cultures of the various types of fungi producing the disease were shown, together with a chart depicting the distribution of the disease in Cleveland.

DISCUSSION

DR. G. W. BINKLEY: There is nothing unusual about these cases, and they are presented before the society to facilitate discussion of some changes my associates and I have made in the treatment of this disease.

The importance of determining the type of fungus in each case was clearly shown by Lewis (Lewis, G. M.: *Am. J. M. Sc.* **189**:364 [March] 1935). He proved that infections of the human type require epilation of the scalp before cure can be effected, while in those of the animal type local applications of tineacides are sufficient.

Instead of relying entirely on microscopic examination of hairs for diagnosis, we now perform culture in each case. Only patients with fungi of the human types are epilated with roentgen rays. The others experience clearing promptly when local applications alone are employed.

I have shown in the chart that nearly all the human types of the disease are confined to more crowded tenement districts inhabited largely by Negroes. Infections of the animal types are contracted chiefly from pet dogs or cats and are shown in our chart to be sporadic over the entire city.

DR. J. R. DRIVER: From Dr. Binkley's study of tinea capitis in Cleveland it becomes perfectly evident why this disease is so rare in private practice. The

condition is seen almost entirely in dispensaries. The animal type of infection is not so common in this community and when it does occur is the result of contamination by pets that are infected. In private practice the condition will usually be of the animal type, while in free clinics the human types predominate.

By careful monthly routine examinations of the scalps of children in the schools in those districts shown in the chart to be the source of this infection it would be possible to hospitalize those infected until they were cured. Within a period of two or three years it should be possible practically to eliminate the human forms of the disease from this city.

DR. C. G. LAROCCO: Dr. Binkley's contribution, I believe, explains why in dispensary practice the condition in some cases responds to local treatment without epilation.

Argyria; Leukoplakia of Tongue. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

J. S., a man aged 65, contracted syphilis many years ago, and leukoplakia of the tongue developed. For two years, starting in 1934, he frequently applied a 20 per cent solution of silver nitrate to irritated areas on his tongue. In May 1936 he stated that his friends remarked a bluish color of his skin.

At present there is a bluish to bluish gray or slate color involving the skin of the entire head and neck and extending to the collar, where it fades perceptibly. The same change is noted on the hands and the forearms. The beds of the nails seem to be especially involved. The mucous membrane of the mouth is affected, the gingival margins being involved most markedly.

The Wassermann and the Kline test was slightly positive.

In a biopsy specimen granules of silver pigment were seen in the basal cells of the epidermis, in the connective tissue in the corium and especially about the sweat glands.

DISCUSSION

DR. H. A. HAYNES (by invitation): In histologic slides from patients with argyria the silver pigment shows up well when examined by dark field illumination.

DR. I. L. SCHONBERG: Dr. L. E. Gaul, of New York, has been successful in demonstrating silver granules in the living epithelium of the salivary ducts. Specimens were obtained by catheterizing the ducts.

Gumma and Syphilitic Osteosclerosis. Presented by DR. GARRETT ARTHUR COOPER.

JOHN E. RAUSCHKOLB, M.D., *President*

March 25, 1937

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

A Case for Diagnosis (Lupus Erythematosus? Lichen Planus?). Presented by DR. E. W. NETHERTON.

L. U., a man aged 57, had mild diabetes mellitus for several years. In April 1936 infected tonsils and abscessed teeth were removed after an attack of hypertrophic arthritis of the right knee.

In September 1935 an itching "pustular" eruption developed on the bearded portion of the face and the right cheek. Shortly thereafter violaceous scaly plaques developed on the bearded portion of the face, on the right cheek below the eye and on the forehead. At the same time small follicular lesions appeared

over the body and the upper extremities. Itching was a troublesome symptom during the early stage.

General physical examination shows nothing relevant. At present on each cheek and the sides of the face there are coin-sized demarcated irregular violaceous plaques, the surfaces of which are rough and slightly scaly and show plugging of the follicles. There is some clearing of the central portions of the lesions, suggesting scarring. Near the outer canthus of and just below the right eye are similar lesions which have a fine adherent gray discoloration. Scattered over the arms, the legs and the trunk are small and large clusters of discrete pinhead-sized acuminate brownish follicular papules which surround a hyperkeratotic plug. The surfaces of these lesions resemble that of a nutmeg grater. Near the spine of the left scapula there is a violaceous plaque similar to the one on the face. This lesion, however, is not sharply defined. On the flexural surface of the left forearm there is a flat angular shiny violaceous papule the size of a large match head. This is surrounded by numerous small follicular papules similar to those seen on the trunk. There are small pigmented areas on the trunk and the arms which have resulted from the involution of the lesions. The vermilion margin of the lower lip shows some dilatation of the follicles near the junction of the cutaneous surface. On the mucous membrane of each cheek there are gun-metal grayish areas and streaks. One lesion on the right cheek is angular. These lesions are surrounded by a bluish areola. The gums around the left lower molars are spongy and tender.

Urinalysis, blood counts and Wassermann and Kahn tests showed no abnormality. Examination of hairs removed from lesions on the face failed to show the presence of fungi. A roentgenogram of the chest showed no evidence of tuberculosis.

Tissue was removed from a cluster of follicular papules on the left elbow in January 1936. Histologic examination showed several layers of hyperkeratotic cells on the surface and no parakeratosis. The granular layer was distinct and consisted of from two to three layers of cells. The rete mucosa was thin and edematous and the basal layer indistinct in places, owing to the edema of the epidermis. In the corium there was marked edema of the papillary layer. The interpapillary pegs were obliterated. The vessels were dilated and surrounded by a slight amount of cellular infiltration consisting of small lymphocytic and connective tissue cells. There were numerous large irregular cells containing large and small granules of a brown pigment, some edema of the corium and little inflammatory reaction below the papillary and subpapillary layers. One section showed hyperkeratotic plugging of the follicles and an inflammatory reaction in the corium just adjacent to the follicle. Cellular infiltration consisted mainly of small lymphocytes and proliferation of the connective tissue cells. The sweat glands were not involved.

Treatment with sodium gold thiosulfate produced marked improvement, but the lesions never completely disappeared.

DISCUSSION

DR. J. R. DRIVER: I thought of three possibilities—lichen spinulosus, lichen planus and lupus erythematosus. I have never seen, heard or read of a case of lichen spinulosus in which there were oral lesions. This man has lesions in the mouth which doubtless are similar or related to the process on his skin. If this condition is ruled out, lichen planus and lupus erythematosus are left. The lesions suggest lichen planus only slightly. However, the condition does not look like lupus erythematosus either. By a process of elimination I should favor lupus erythematosus.

DR. H. J. PARKHURST, Toledo, Ohio: I agree with Dr. Driver. I feel that the lesions on the face are probably those of lupus erythematosus which has largely subsided.

DR. E. W. NETHERTON: I saw this patient some time ago and felt that he had lupus erythematosus. He dropped out of sight and returned recently because of

some recurrence of lesions on his face. These have practically disappeared under therapy with a gold preparation. There are several interesting features about this case. For instance, the color of the lesions is different from that of any I have seen in lupus erythematosus. The lesions have always been purple blue. The patient states that the condition started as a pustular eruption on the face and rapidly turned into the plaques that are present now. The eruption is suggestive of lichen spinulosus clinically, and the lesions are grouped as in that disease, but there are no lesions on the back of the hand. Lichen scrofulosus associated with lupus erythematosus has to be considered, but that condition is not inflammatory as a rule. The lesions in the mouth are not suggestive of leukoplakia, and the lesion on the left forearm is flat, shiny, angular and papular and suggestive of lichen planus. The fact that the lesions responded to a gold preparation made me favor lupus erythematosus. As far as I know, lichen planus does not respond to therapy with gold compounds. Sometimes the only way lichen planus can be distinguished clinically from lichen spinulosus is by the presence of flat shiny papules. Otherwise the two conditions have the same clinical characteristics. I am going to take some more biopsy specimens if the patient will permit it.

DR. H. N. COLE: Some cases of lichen planus atrophicus have been reported in which there are associated lesions of lichen scrofulosus on the body, and I believe the entire picture here can be placed in that category. With that condition there may be pigmentation of the sort seen here. The typical lesions of lichen planus on the forearm would go well with that diagnosis. It is well known how stubborn the process is as far as therapy is concerned. The histologic picture of this section would fit in all right with that of an atrophic type of lichen planus.

DR. E. W. NETHERTON: The only similar case that I remember observing was presented by Dr. C. J. Shepard at a meeting of this society several years ago. It was that of a man with lesions on his face similar to these, and the lesions on the body were accepted as lichen planus. The lesions on the face were almost dark purple and similar to these. The picture here is striking. I have felt for the last few months that it is lichen planus.

DR. H. J. PARKHURST, Toledo, Ohio: When I see scarring, I am inclined to think of lupus erythematosus and not of lichen planus. I have never seen scarring of the mucosa from lichen planus, as far as I can recall.

DR. E. W. NETHERTON: I do not think there is much, if any, scarring in the lesions in the mouth.

Dermatophytosis (from a Horse). Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

T. S., a man aged 24, while taking care of a sick horse which had lost hair from the head and neck, about four weeks ago, noticed two circular scaly lesions on his neck. These increased in size and tended to clear in the center. Subsequently numerous smaller lesions of the same character developed on his face, his neck and his arms. These are rosy, spread at the periphery and have fine branlike scaling in the center.

Microscopic examination of scrapings revealed a fungus. Cultures on Sabouraud's medium showed Megalosporon equinum.

DISCUSSION

DR. JOHN A. GAMMEL: This type of fungous infection is interesting and not often seen.

Hutchinson and Boeck's Sarcoid. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

S. J., a well nourished Negress aged 36, states that about five years ago an infiltrated mass about 4 cm. in diameter developed in the right upper quadrant of the abdomen. One year ago a dull red granulomatous lesion 2 cm. in diameter developed on the tip of her nose. There are several pinhead-sized papules at the

border of this lesion. At about the same time the upper lip became swollen and diffusely infiltrated. On the under-surface of the lip there are two reddish white plaques about 1 cm. in diameter. Three months previous to presentation swellings resembling spina ventosa developed on several of her fingers.

Roentgenograms showed cystic changes in the bones of the involved digits and increased density and mottling throughout the right lung with an infiltrate in the region of the hilus. The pleura was thickened throughout both lungs, and at the base of the right lung there was a nodular area of increased density about 1.5 cm. in diameter. Serologic tests for syphilis were negative. Blood and differential counts and a hemoglobin determination showed no abnormality. The cholesterol content of the blood was 258 mg. and the uric acid content 4.2 mg. per hundred cubic centimeters. Reactions to tuberculin of human and bovine types with dilutions of 1:10,000 were negative and with dilutions of 1:1,000 were 2 plus.

Biopsy showed the epidermis to be thin and the cells swollen with edema. The interpapillary pegs were gone. Throughout the corium at all depths were rather sharply delimited nodules of unusual cells. These nodules were marked off by connective tissue septums. Next to the septums a few lymphocytes were found, but in most areas the lymphocytic reaction was absent. The mass of the nodules was made up of swollen, almost liquefied epithelioid cells, the nuclei of which were large and vesicular. In the deepest nodule of this section were two giant cells.

DISCUSSION

DR. E. W. NETHERTON: I think the lesion on the nose is miliary lupus. The swellings of the fingers are soft. I wonder if the condition is not tuberculosis.

DR. H. N. COLE: The patient has an infiltrate in the right hilus which is suggestive of sarcoid. It is difficult to say much about the nasal lesions. The lesions on the inside of the lower lip are interesting. They are raised, rather pearly, reddish white and about the size of the nail of the little finger. I do not think the histologic picture characteristic of sarcoid. I believe there is a suggestion of foam cells, such as are seen in xanthoma, and there is a high cholesterol content in the blood. In addition there is no anergy to tuberculin.

DR. G. W. BINKLEY: In answer to Dr. Cole's objection that a diagnosis of Boeck's sarcoid is not justified or is made less likely by this response to tuberculin, I should suggest that the period of the disease in which complete anergy to tuberculin is found is at an end and that cutaneous allergy is now developing during a phase of improvement in the sarcoid process. This cyclic change in cutaneous allergy has been fully described by Jörgen Schaumann. The nodules seen in the histologic specimen may or may not contain epithelioid cells. I did not see any foam cells. I felt that the general picture as seen in the slide was consistent with a diagnosis of sarcoid.

Primary Systemic Amyloidosis. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

A. B. is a well developed and well nourished woman aged 62. Eight years ago she noticed a slight swelling of her left wrist. This has gradually enlarged to about the size of a small orange. During the past two years her tongue has become enlarged, and nodules have formed on the dorsum. Similar nodules developed at the same time on the mucous membrane of the lips. In July 1935 she sustained a spontaneous fracture of the neck of the left femur. She has no discomfort but has been unable to walk because of the fracture.

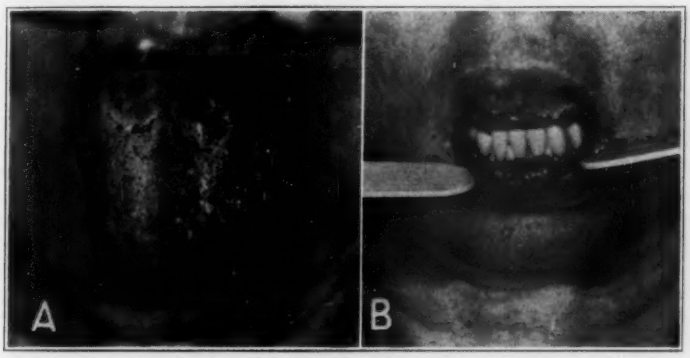
Examination shows the tongue to be considerably enlarged, with several pea-sized or larger yellowish nodules (fig. *A*) on the dorsum. Similar nodules are present on the inner surfaces of the lips (fig. *B*). The deeper structures of the lips are infiltrated by cuboidal yellowish masses. About the tendons of the ankles, the wrists and the hands there are infiltrated diffuse masses.

Vaginal examination reveals yellowish plaques on the vaginal wall.

The Wassermann test and blood and differential counts showed no abnormalities. There were 12.5 mg. urea nitrogen, 235 mg. cholesterol, 4.2 mg. phos-

phorus, 9.5 mg. phosphatase and 9.4 mg. calcium per hundred cubic centimeters of blood. The dextrose tolerance test showed traces of sugar in the urine after two or three hours. The sugar content of the blood was 98 mg. when the patient was fasting and 186 mg. at one hour, 220 mg. at two hours, 128 mg. at three hours and 184 mg. at four hours after ingestion of food. The fat content of the blood was 1.17 per cent.

A biopsy specimen from the left wrist stained by the Van Gieson method and with scarlet red showed a tendon in which a large portion of the connective tissue was replaced by lipoid-like material. There was no inflammatory reaction, and there were no foam or giant cells. No crystals were found when the specimen was examined under polarized light. A biopsy specimen from a nodule on the lower lip stained with iodine and later with sulfuric acid and with methyl violet indicated



Primary amyloidosis: *A*, many papules the size of a split pea on the moderately enlarged tongue; *B*, three yellowish nodules on the lower lip.

that the homogeneous mass was mostly amyloid. On the other hand, the tests for fat with osmic tetroxide and sudan III gave negative results with the amorphous material, but in the middle of the masses and around the capillaries one could detect many tiny droplets of fat, giving the characteristic reaction of neutral fats. Whether the fat was primary or secondary to the amyloid infiltration could not be determined.

DISCUSSION

DR. H. N. COLE: I think the macroglossia, the peculiar yellow lesions on the tongue and the absence of chronic infection are characteristic of primary amyloidosis.

JOHN E. RAUSCHKOLB, M.D., *President*

April 22, 1937

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

Superficial Basal Cell Epitheliomatosis; Arsenical Keratoses of Palms and Soles. Presented by DR. JOHN E. RAUSCHKOLB for DR. E. J. ARDAY, Lakewood, Ohio (by invitation).

B. L., a man aged 49 years, states that an eruption developed on his face and scalp twenty-five years ago and that it was diagnosed as psoriasis. It has been

treated with salves, and a solution of arsenic has been taken internally off and on until recently.

About eight years ago lesions which he regarded as psoriasis began to develop on his body. He did not consult a physician but continued treatment with the salves and the arsenic preparation previously prescribed.

The eruption at present is limited to the trunk and the upper extremities and consists of numerous (perhaps fifty) lesions varying in diameter from a few millimeters to 8 cm. A typical lesion has a sharply defined fine pearly border, while the center is erythematous and scaly or crusted and shows some atrophy and telangiectasia. Removal of crusts from some advanced lesions reveals a granulomatous ulceration.

Three of the proliferating lesions were removed for biopsy; their bases were cauterized and subsequently irradiated (400 roentgens unfiltered every other day for ten treatments for a total of 4,000 roentgens). Seven smooth lesions were treated with solid carbon dioxide. One lesion in the perineal region was electrodesiccated during anesthesia with procaine hydrochloride. All lesions have responded satisfactorily to treatment.

The palms and soles present numerous small horny hyperkeratotic lesions.

Biopsy showed that the epidermal architecture was greatly disturbed. The normal outline of the rete pegs was lost in many places, and the epidermis was considerably thinned. Mitotic figures were numerous throughout the epidermis, and there was a comparative thickening of the stratum granulosum. At one point there was a collection of deeply stained cells outlined by rows of cells of the basal type. This collection of cells did not invade the cutis. Biopsies of the tumor-like lesions showed collections of basal cells throughout the cutis in finger-like projections separated by fine trabeculae of young connective tissue.

DISCUSSION

DR. E. W. NETHERTON: I think the condition is unusually extensive in this case. I see no lesions which at the present time resemble psoriasis.

DR. H. J. PARKHURST, Toledo, Ohio: I have observed several cases of this disease in which there was a history of psoriasis and in which arsenical treatment had been given previously. There must be some relation between arsenical therapy and the development of these lesions.

DR. J. R. DRIVER: Dr. Cole and I have had several cases in which the condition has developed in association with psoriasis. In some instances the malignancy is of the prickle cell variety.

DR. E. J. ARDAY, Lakewood, Ohio (by invitation): The members are all familiar with the work of Montgomery on this subject. He has described cases in which no arsenical therapy had been previously received. In those instances in which arsenic had been given the epitheliomas were, I believe, always of the prickle cell type. There seems to be considerable controversy regarding the role that arsenic plays. Some investigators believe that the lesions develop as a result of an inherited predisposition rather than of arsenical treatment.

Oriental Sore ("Aleppo Boil"). Presented by DR. H. N. COLE and DR. J. R. DRIVER.

Mrs. G. K., an American aged 35, was born in Syria. While on a trip to the Near East a year ago, she remembers having been bitten by sand flies in Bagdad. About two months later a sore appeared on each forearm. These have slowly increased in size and shown no tendency to heal. The patient feels well otherwise.

On the right forearm there is a sharply defined nodule about 2 cm. in diameter, slightly raised above the surface, slightly reddish and with a little scaling on its surface and a suggestion of an opening at the apex of the area. It is not partic-

ularly painful. There is no evidence of pruritus. On the flexor surface of the other forearm is a smaller, similar lesion, 0.5 cm. in diameter.

General physical examination shows no abnormality.

Smears from the two lesions, stained with Wright's stain, showed typical grouped oblong Leishmania tropica.

A biopsy showed slight hyperkeratosis and parakeratosis of the epidermis. In the corium were dense areas of infiltrate made up of epithelioid and plasma cells, mononuclears and fibroblasts. Certain of the cells showed a tendency to vacuolar degeneration. While no parasites were identified in the tissues, numerous small deeply staining round bodies about 2 microns in diameter were observed. The tissue showed much edema and frequent giant cell formation.

Therapy with roentgen radiation and intravenous injections of fuadin has been started.

DISCUSSION

DR. H. G. MISKJIAN: I am an Oriental and have previously observed just one case of this disease. It is seen especially in Syria and Mesopotamia. The histologic section was characteristic of the disease.

DR. JOHN E. RAUSCHKOLB: Will this infection establish permanent immunity?

DR. J. R. DRIVER: I have recently read an article on this disease which stated that immunity is not produced.

DR. H. N. COLE: Without the patient's history, I doubt if any one would have considered the diagnosis of Aleppo boil. All that we had to assist us was the history, the chronicity and the long duration of the condition and the fact that it appeared to be a trivial lesion that did not heal like a manifestation of an ordinary infection. We were suspicious since the patient had taken a trip to the Near East, and had been bitten by insects while there. The laboratory examinations confirmed our suspicions.

Pemphigus. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

B. L., a woman aged 42, noticed some painful sores in her mouth in February 1937. About three weeks later a generalized eruption developed on her body associated with fever and marked malaise for the past ten days.

There is a symmetrical extensive generalized eruption of many lesions on the anterior part of the trunk and the extremities. At the time of her first examination there were many annular and iris-formed erythematous patches and all sizes of bullae and vesicles appearing on the apparently normal skin. Nikolsky's sign was not present. Many flaccid bullae had ruptured, exposing a moist bleeding surface. The most severe involvement is on the lips, the oral mucosa, the anterior surface of the trunk, the upper and lower extremities and the groin.

I considered her condition to be erythema multiforme and prescribed the routine treatment with salicylates, which produced no benefit. Her temperature was approximately 40 C. (104 F.).

The differential blood count showed 12 per cent eosinophils; otherwise examinations of the blood and urine showed no abnormality. One culture of blood showed no organisms.

Treatment with iron cacodylate and a hemostatic preparation was instituted two days before presentation.

DISCUSSION

DR. J. E. EDGAR FISHER: I agree with the diagnosis of pemphigus.

DR. J. R. DRIVER: When this patient first entered the hospital the eruption resembled erythema multiforme closely. The patient was not so ill as she is now, but therapy with salicylates produced no response. The disease has become progressively worse; the fever is higher, and my associates and I now consider pemphigus the most likely diagnosis. Because of the evidence of an acute infectious disease I believe the use of sulfanilamide should be considered.

DR. E. W. NETHERTON: Dr. M. C. Welch, of the Mayo Clinic, feels that pemphigus may be due to a streptococcus. If this is true, it might be interesting to try sulfanilamide.

DR. H. G. MISKJIAN: Since no one has objected to the diagnosis, I beg to do so. The condition does not look at all like pemphigus. The patient who has pemphigus has a normal skin where there are no bullae. In this case there is a definite inflammatory reaction. The patient has a fever, and the fact that there is a group of bullous diseases of infectious origin with a definite febrile course must not be lost sight of.

DR. H. N. COLE: There are many physicians, especially of the Vienna school, who think the differentiation between dermatitis herpetiformis and pemphigus is an artificial one. The members have all observed cases in which one makes one diagnosis at one time and another one at another time. I agree with Dr. Driver that several bullous lesions appeared on perfectly normal skin. I am of the impression that this case is one of pemphigus, for the patient looks too ill for her condition to be dermatitis herpetiformis.

A Case for Diagnosis (Dermatitis Herpetiformis? Erythema Exsudativum Multiforme?). Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

M. S., a frail man aged 57, has been troubled with an intensely itching cutaneous eruption for one year. There have been periods of partial remission, but the eruption has never completely disappeared.

There are many acute lesions which have gone through stages of urticarial edema, vesiculation and finally subsidence of the inflammatory process to a brownish desquamation of the epidermis. The efflorescences are located on the extensor surfaces of the forearms and the hands, the outer scapular regions, the buttocks and the outer surfaces of the lower extremities.

The primary lesion is an urticarial wheal accompanied with vesicles of all sizes. The urticaria is in arciform arrangement, and the reaction as a whole shows grouping in the areas involved. There is no residual pigmentation.

Serologic examination of the blood for syphilis gave negative results. The blood pressure was 150 systolic and 80 diastolic. There were 3,000,000 erythrocytes and 70 per cent hemoglobin. The differential cell count showed all forms of cells to be within normal limits.

Histologic examination of a specimen of skin from the anterior aspect of the thigh showed an epidermal vesicle on a rete Malpighii which was remarkably free from pathologic change. There was moderate edema in some of the papillae. Around the vessels was a moderate amount of lymphocytic infiltrate accompanied with a few eosinophils.

After the administration of 10 grains (0.65 Gm.) of acetylsalicylic acid every three hours until the patient became toxic the response was immediate and remarkable. After four days the inflammatory reaction had subsided completely.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: The evidence in this case favors a diagnosis of dermatitis herpetiformis, at least at the present time, although I recall having observed at least one case in which the condition appeared to change from erythema multiforme into typical dermatitis herpetiformis.

DR. E. W. NETHERTON: I think the lesions have changed, so that it is difficult to form an opinion. I favor a diagnosis of possible erythema multiforme, because there is no pigmentation and no scarring, and there has been definite improvement following therapy with salicylates. There is little erythema. The patient is anemic and undernourished, and I wonder if there is some systemic condition—perhaps malnutrition—that contributes to his cutaneous condition.

JOHN E. RAUSCHKOLB, M.D., *President*

May 27, 1937

C. L. CUMMER, M.D., *Secretary*

J. R. DRIVER, M.D., *Reporter*

Precocious Tertiarism in Early Syphilitic Relapse. Presented by DR. G. W. BINKLEY (from the Department of Dermatology and Syphilology, the City Hospital).

A. P., a man aged 36, had a generalized secondary eruption of syphilis in May 1936. He received treatment with an arsenical preparation intravenously and injections in the hip for one month only. Approximately one year later, in May 1937, he was admitted to the hospital with an extensive eruption.

General examination shows annular and serpiginous papular lesions on the face, the upper part of the chest and the back. The lesions show central healing and progression at the borders. The largest area involved is on the right shoulder, where the lower border shows ulceration and crusting. Smaller (dollar-sized) areas on the back are almost completely healed. The skin of the healed lesions is soft, smooth and pliable, without anetoderma. On the under-surface of the tip of the tongue is a round mucous patch the size of a quarter.

The Wassermann and the Kline test were strongly positive. The spinal fluid showed a moderately positive reaction to a globulin test, and the Wassermann reaction was strongly positive with 1 cc. of fluid. The cell count and colloidal gold curve showed no abnormality.

A biopsy specimen from a cutaneous lesion showed changes consistent with a diagnosis of syphilis.

DISCUSSION

DR. H. N. COLE: This patient was shown to illustrate a type of relapse in syphilis. The eruption is more or less generalized yet has many of the characteristics of late syphilis of the skin. There is, in addition, an involvement of the central nervous system.

Scleroderma (Sclerodactylia; Atrophic Arthritis; Silicosis Pseudoxanthoma Elasticum?). Presented by DR. E. W. NETHERTON.

A. B., a man aged 48, had the diseases of childhood but no other serious illness. From 1914 to 1919 he worked in a brick yard, where the atmosphere was laden with particles of silica.

Two years ago, after the removal of several infected teeth, he began to notice a sensation of tingling in the tips of his fingers. This was not associated with discoloration or other visible changes in his skin. Six months later the joints of the fingers became large and painful, and the skin began to appear glossy. Off and on since then he has had ulcerations over the joints of the hands, the tips of the fingers and the elbows. He has lost 50 pounds (22.7 Kg.) since the onset of the illness. There has never been any local asphyxia or syncope, such as is seen in Raynaud's disease.

The patient is well developed and fairly well nourished and has a fixed masklike expression of the face. Physical examination revealed that little was abnormal besides the cutaneous lesions.

The skin on the fingers and the dorsal surfaces of the hands is smooth, glossy, brownish pink and sclerotic. The joints of the fingers are enlarged and slightly pink, and there are a few small chronic, crusted ulcers and hyperkeratotic lesions on the tips of the fingers and over the joints of the hands. On the back there are large poorly defined slightly edematous smooth brownish red areas. On the side of the neck and the upper part of the chest in the region of the clavicles there are

yellowish streaks and papules which do not seem to be as thickened and sclerotic as the skin of the hands. The skin of the face and the forehead is somewhat sclerotic.

A roentgenogram of the chest showed pulmonary tuberculosis secondary to silicosis and fibrous infiltration at the hilus, general interstitial and nodular infiltration, more marked in the middle portion, and small areas of exudative infiltration at the apex of the right lung. The left lung appeared similar to the right.

A roentgenogram of the right hand showed general demineralization and rheumatoid arthritic change of the midphalangeal joints. There was a small cystic area at the distal end of the first phalanx of the second finger. A determination of gastric acidity after ingestion of the Ewald test meal showed free acid 38 and total acid 59. The sedimentation rate was 2 mm. per minute. Blood counts and a determination of blood sugar showed no abnormality. The Wassermann and the Kahn test were negative. The calcium content of the blood was 9.6 mg. per hundred cubic centimeters. Examination of the urine showed no abnormality. The basal metabolic rate was +19 per cent.

Biopsy showed the epidermis to be somewhat thinned, and in places the interpapillary spaces were obliterated. There was a slight amount of hyperkeratotic scaling on the surface of the section. The papillary layer showed a slight amount of edema; the vessels were moderately dilated and surrounded by a mild degree of infiltration of small cells. There was a marked increase in the amount and the density of the collagen of the corium proper, and the sweat glands and sebaceous glands were sparse. With the hematoxylin and eosin stain the number of blood vessels in the corium appeared diminished, and the staining of the corium varied in intensity throughout the section. With Weigert's stain fragmentation of the elastic tissue fibers appeared marked in the midportion of the corium and not so marked in the papillary layers.

Recently procaine hydrochloride was injected into the right cervicodorsal ganglion, and bilateral cervicodorsal ganglionectomy was performed. To date there has been no noticeable improvement.

DISCUSSION

DR. JOHN A. GAMMEL: I do not see any evidence of pseudoxanthoma elasticum.

DR. H. N. COLE: It seems to me that the patient is beginning to show a certain amount of infiltration of the buccal surfaces and presents the picture of progressive scleroderma.

DR. E. W. NETHERTON: There was some question in my mind as to whether the condition might be pseudoxanthoma elasticum instead of scleroderma, because the cutaneous changes were not markedly sclerotic, and the section showed fragmentation of the elastic tissue fibers. There were no angioid streaks in the retina.

Dermatosis Industrialis (Acneform Type). Presented by DR. H. N. COLE and DR. J. R. DRIVER.

E. E., a man aged 21, has been employed for the past year as an assistant chemist in a research laboratory devoted to the analysis of commercial oils. The chemical process consists chiefly of chlorinating hydrocarbons. He states that he had no cutaneous trouble until three months ago.

Involving the skin of the face, the ears, the neck, the upper part of the chest, the shoulders, the back, the thighs and the buttocks is an extensive eruption consisting of countless comedonous, pustular, papular and cystic lesions of acne.

DISCUSSION

DR. MAURICE SULLIVAN, Baltimore: This case demonstrates clearly the production of an acneform eruption and suggests what may be one of the factors in causing acne vulgaris. In trying to work out some therapy I have spoken to a chemist, who suggested that perhaps, in addition to other precautions, the worker might put a coating of grease or oil on the skin and that the chlorinated hydrocarbons might be dissolved in the grease and not get into the skin.

DR. M. J. GIBANS, Akron, Ohio: How can the acneform lesions on his legs be explained?

DR. MAURICE SULLIVAN, Baltimore: The chlorinated hydrocarbons go right through the clothes, producing an irritation. The patient then scratches and rubs it in.

DR. JOHN E. RAUSCHKOLB: This condition is common in men who work on machines where oil splashes.

DR. H. N. COLE: My associates and I have been much interested in this problem and have seen four patients with this condition from this one laboratory. All are in a group of chemists studying various types of oil. The same type of eruption has developed in all.

Questionable Lupus Erythematosus. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

McK. H. L., a man aged 46, states that in the early spring of 1936 a lesion developed on the left side of the face and was diagnosed as ringworm. It gradually healed with local treatment. In March 1936 a lesion developed on the right side of the neck and has continued to date. There are few or no subjective symptoms.

Physical examination shows him to be well developed and well nourished.

There are a few papular lesions on the left cheek, while on the right side of the neck well down below the jaw, there is an ovoid area about 1½ by 1 inch (3.8 by 2.5 cm.). The edges show the skin to be rather like cigaret paper, somewhat thickened but definitely atrophic. Just inside this is a light reddish area the size of a pigeon's egg, slightly edematous, raised above the surface and showing telangiectasia and numerous prominent follicular plugs.

The patient has many bad teeth.

The laboratory examinations showed nothing abnormal.

Biopsy showed a slightly distended and perhaps slightly atrophic epithelium. There was no hyperkeratinization, but parakeratotic follicular plugs were present. The corium showed some edema and a few blood vessels but no hyperemia. There was no marked cellular infiltrate and no perivascular collection of cells. The section was not typical of lupus erythematosus, although it was not necessarily inconsistent.

Weigert's stain showed some degeneration and dissociation of the elastic tissue in the upper part of the right and the left third but not the middle third of the corium.

With Van Gieson's stain no degenerated colloid masses were evident in the upper part of the corium, and the elastic tissue showed no colloid degeneration. The picture there included (1) a distended and atrophic epithelium without hyperkeratinization, (2) degeneration and dissociation of connective tissue, with elastic tissue in the upper part of the corium and no cellular infiltrate and (3) some swelling and degeneration of collagen in the lower part of the corium.

Livedo Reticularis Due to Syphilis. Presented by DR. E. W. NETHERTON.

C. B., an obese woman aged 36, for the past ten years has noticed increased mottling of the skin on the arms and the legs, which was particularly marked during the winter. In 1930 she consulted a physician, who has treated her intermittently for syphilis. She has no knowledge of when she contracted syphilis.

On the cutaneous surfaces of the hands, on the extensor and the flexural surfaces of the arms and to some extent on the lower extremities there is a reticulated, erythematous discoloration which corresponds with the vascular network of the skin and which can be obliterated by pressure. There are no subjective symptoms and no infiltration or clinical signs of an inflammatory reaction in the involved skin.

There were no abnormal neurologic changes and the general physical examination showed no abnormality with the exception of a moderate enlargement of the heart and the presence of a faint systolic murmur in the aortic region.

A roentgenogram of the chest showed considerable fibrosis at the hilus and pulmonary fibrosis of both lungs and a large heart. Spinal puncture showed no cells or globulin, 25 mg. total protein and negative Wassermann and colloidal gold reactions. The Wassermann reaction of the blood was strongly positive, and the Kahn test 2 plus.

The biopsy revealed a moderate amount of edema in the papillary layer, associated with dilatation of the vessels throughout the corium. The most noteworthy change was around the vessels in the cutis and consisted of a mild perivascular lymphocytic infiltration, edema of the endothelium and some thickening of the other layers of the vessels. Around each dilated vessel there was a zone in which the fibers were fragmented and edematous and took a bluish red stain. This was particularly noticeable in the larger vessels in the corium.

DISCUSSION

DR. BENJAMIN LEVINE: This condition is a good example of livedo reticularis, seen not infrequently in syphilitic vascular disease.

DR. H. N. COLE: The lymphocytic infiltration around the vessels seen in the biopsy specimen was striking and confirms the hypothesis of syphilitic origin.

Stomatitis and Cheilitis Due to Dental Plates. Presented by DR. H. N. COLE and DR. J. R. DRIVER.

A. E., a Jewess aged 66, complains of a sore mouth and lips of several years' duration, with periods of partial remission. The present exacerbation started about three weeks ago and has been unusually severe. Her general health otherwise has been fairly good. For the past fourteen years she has been wearing the same upper and lower dental plates. She is not in the habit of removing the plates during the night.

There is severe cheilitis of the upper and the lower lip, redness, scales and cracks, with blood crusts. Located on the hard palate and limited sharply to the area covered by her dental plate is marked stomatitis, showing redness, exfoliation and superficial ulceration. A similar condition, although less severe, is present on the lower alveolus in the area covered by the lower dental plate. There is no evidence of vitamin deficiency.

On the flexor surface of the right forearm, where the upper dental plate was bandaged in place for twenty-four hours, there was a severe vesicular reaction, with considerable redness and some edema. Another patch test using scrapings from the lower plate produced a similar positive reaction.

DISCUSSION

DR. G. W. BINKLEY: I should like to ask the presenters if the irritating substance in the dental plate has been determined.

DR. C. L. CUMMER: I want to say one thing about stomatitis caused by dental plates. A negative patch test cannot be relied on. I have had a patient with definite stomatitis, which cleared when the plate was left out of the mouth. I put it back, and the condition recurred. I did this several times before I could satisfy her own dentist. Yet the patch tests on the skin were negative. It is strange that the patient presented today should have had freedom from irritation for so many years.

DR. BENJAMIN LEVINE: Mercury is often incorporated in the rubber, and it is possible that this is responsible for the stomatitis in these cases.

DR. E. W. NETHERTON: This case calls to my mind the dermatitis that occurs sometimes from rubber gloves. Obermayer, I believe, found that if rubber gloves are soaked in a normal solution of sodium hydroxide for twenty-four hours they cease to produce dermatitis, and patch tests with the treated gloves are negative. At the Cleveland Clinic Foundation Hospital this finding has been tested and proved during the last three months. It would be interesting to use this treatment on the dental plates of this patient.

Granuloma Annulare. Presented by DR. E. W. NETHERTON.

J. H., a well developed and well nourished girl aged 13, in 1932 had measles complicated by bilateral otitis media, which required mastoidectomy. When she was 7 years old her mother noticed a few small papules on each elbow. These have gradually increased in number, but have remained stationary in the past few years. There are no subjective symptoms. Recently a small papule has developed on the right heel near the achilles tendon.

On the right elbow there is a cluster of smooth cutaneous papules varying in size from that of a match head to that of a split pea. The lesions are well defined and have a doughy consistency. A few of them have become confluent to form small plaques, some of which show slight central umbilication or a tendency to form ring-shaped lesions. On the left elbow there is a linear incision, the result of recent removal of a biopsy specimen. After the taking of the biopsy specimen all the lesions on the left elbow promptly disappeared.

Blood counts and a hemoglobin determination gave normal results. The Wassermann reaction was negative. The cholesterol content of the blood was 147 mg. per hundred cubic centimeters. The reaction to human tuberculin (Mantoux 0.01 mg.) was positive. A roentgenogram of the chest showed fibrous and calcified infiltration of the hilus with extension well out into the upper lobe in the right lung. The left lung showed some fibrosis at the hilus. This was interpreted as an infantile type of pulmonary tuberculosis.

Biopsy showed moderate acanthosis. The papillary and the subpapillary layer were edematous. The vessels were somewhat dilated and surrounded by a marked infiltration consisting of lymphocytes and epithelioid cells. Deeper in the corium there were larger areas of cellular infiltration, some consisting almost entirely of epithelioid cells while others were made up of epithelioid cells and lymphocytes. Occasional polymorphonuclear neutrophils could be seen throughout the areas of infiltration. This inflammatory reaction was present to some degree around the sweat glands and the hair follicles. In one portion of the section, near the periphery of a large area of infiltration consisting mainly of epithelioid cells, there was a rather large area of necrosis.

DISCUSSION

DR. R. E. BARNEY: I agree with the diagnosis of granuloma annulare. In this case it is interesting to note the disappearance of the lesions in the region of the scar from the biopsy. I have noted a similar curative effect in other cases and can recommend removal of a specimen as a therapeutic procedure.

Urticaria Pigmentosa (Acquired Type). Presented by DR. E. W. NETHERTON.

S. L., a housewife aged 30, had tuberculous osteitis of the right foot at the age of 3 years and typhus at the age of 15. For the past several years she has had no serious illnesses. Two years ago small brown spots began to appear on the arms and the abdomen, and these have increased in number until now the whole body, with the exception of the face, the neck, the palms and the soles, has become involved.

The lesions are grouped flat brownish macules the size of a match head scattered over the trunk and the upper and lower extremities. When any of the lesions are irritated they become reddened, slightly edematous and moderately pruritic.

Routine laboratory examinations of the blood, including blood counts, a hemoglobin determination and the Wassermann test, showed no abnormality.

The biopsy showed marked thinning of the epidermis, with a slight amount of hyperkeratosis of the surface in the section. There was considerable edema of the papillary and the subpapillary layer, and in the upper part of the corium and in the papillary layer there were narrow strands of perivascular infiltration consisting of small lymphocytes and mast cells with a few fibroblasts. No free pigment was seen in the corium, and there was no noticeable increase in pigment in the basal layer of the epidermis. A section stained with Ehrlich's stain for mast cells

showed numerous large irregular granular cells scattered throughout the small amount of perivascular infiltration in the corium. The granules stained blue.

The patient was started on treatment with iron and vitamin C in the form of cevitamic acid.

Dyskeratosis Naevica. Presented by Dr. John A. Gammel.

T. T., a man aged 20, of Italian descent, states that changes developed in his skin when he was about 4 years old. These changes have persisted practically unchanged.

The eruption is limited entirely to the right side of his body and is most marked at the nape of the neck, where the cutaneous follicles are elevated, pointed and surrounded by a brown halo. The skin between the lesions shows no change. The plugs closing the follicles can be removed with forceps. Some of these plugs have a length of 2 mm. and leave a small, occasionally bleeding crater which after a few weeks fills up again with horny material.

There is another less markedly developed patch, reaching from the midline of the back to the angulus scapulae. More diffuse changes of similar character are noted over the shoulder, below the clavicle and on the anterior aspect of the neck.

Biopsy showed a nonuniform type of hyperkeratosis. The excess keratohyalin was in the form of rounded masses, which occupied a series of deep and shallow concave depressions which approximated one another closely. Some of these could be oriented in relation to hair follicles and gland ducts, but others appeared to be independent of natural openings. There was no parakeratosis. Some of the rete pegs appeared to have been obliterated, while in other places they were long, narrow and irregular. There was considerable focal disorganization of the epidermis, especially in the cells beneath the keratohyalin plugs. Here the cells were frequently large, with extremely vesicular cytoplasm and nuclear degeneration. Some of the degenerate nuclei appeared unusually large and hyperchromatic, whereas others were pyknotic. Coarse basophilic granules were seen in the degenerated cells.

Where the degenerative process affected many contiguous cells, the individual cells were polyhedral. There was considerable nuclear variation, most pronounced in the deeper layers of the epidermis, where there were many "pencil cells." No intra-epidermal defects of the type commonly seen in Darier's disease were present. There was sparse periglandular and perivascular mononuclear infiltration of the corium.

DISCUSSION

Dr. H. J. Parkhurst, Toledo, Ohio: I did not examine the sections, but I think that the clinical appearance of the follicular lesions and their unilateral linear distribution are in favor of a diagnosis of follicular nevus.

Dr. J. R. Driver: I think C. J. White was the first to describe this condition under the name naevus follicularis keratosus.

Dr. John A. Gammel: The histologic picture in many ways resembles Darier's disease. Darier's disease is at times seen in connection with nevi.

LOS ANGELES DERMATOLOGICAL SOCIETY

Harry P. Jacobson, M.D., *President*

April 13, 1937

Thomas W. Nisbet, M.D., *Secretary*

Diffuse Alopecia. Presented by Dr. Nelson Paul Anderson.

F. E., a white woman aged 30, presents a marked generalized thinning of the hair over the entire scalp. What few hairs remain are from ½ to ¾ inch (1.3 to

1.9 cm.) in length. There is no scaling of the scalp. No keratosis pilaris is present.

The Wassermann reaction was negative. Examination of the hairs showed no fungi.

The patient has been treated with a mild ointment of sulfur and salicylic acid.

DISCUSSION

DR. SAMUEL AYRES JR.: The condition is a type of toxic alopecia. According to the patient, the present attack was not preceded by fever. There might be some chronic focus of infection which precipitated this attack, which is taking the form of diffuse rather than localized alopecia. I have seen both diffuse alopecia and alopecia areata after acute infections. During the epidemic of influenza in 1918 I had an opportunity to follow a number of cases of postinfluenzal alopecia. Both types were noted.

DR. H. C. L. LINDSAY: I think this condition is a subthyroid type of alopecia areata. The patient has cold hands and poor circulation of the extremities. In the subthyroid type of alopecia areata the response to treatment with thyroid is usually rapid.

A Case for Diagnosis (Dermatitis Herpetiformis). Presented by DR. PAUL D. FOSTER, for DR. A. F. HALL JR. (by invitation).

This patient is a Russian Jew aged 52, with a dark complexion. The entire cutaneous surface except that of the face, the scalp, the hands, the feet and the genitalia is involved. The eruption consists of round and oval dry, sparsely scaly plaques which show light infiltration and are slightly hyperemic. The long axis of the oval lesions lies in the lines of cleavage. In and around the axillae and the groins there is complete confluence of the lesions, which exhibit a definite violaceous hue. There are a few scattered pinhead-sized pustules on erythematous bases, several on the right flank being close enough to be considered a loose group. The patient designates these as the primary type of lesion. He says that after rupture these pustules (rarely vesicles) change to the plaque type of lesion now in evidence in most places. The histologic examination showed a picture consistent with dermatitis herpetiformis.

The eruption began in 1914 under the arms, then spread elsewhere on the body. It has always been worse in May, June and July and then clears gradually and remains clear during the winter. The present attack began in March, and the condition is now getting worse. The patient is losing weight. The itching is now slight and is never marked. Roentgen and ultraviolet irradiation have been employed without noticeable effect. The eruption never affects the face, the genitals or the palms; the soles have been affected once. The mucous membranes remain clear.

DISCUSSION

DR. SAMUEL AYRES JR.: I agree with the diagnosis of dermatitis herpetiformis because of the marked symmetry of the lesions, their tendency to vesiculation around the edges, their recurrence and their pronounced itching.

DR. JOSEPH WEINBERG (by invitation): The condition might be erythema multiforme, for rare types of lesions of this disease are seen.

DR. KENDAL P. FROST: The condition presents characteristics which suggest both dermatitis herpetiformis and pustular psoriasis. I am rather inclined to the latter diagnosis, although observation over a period and biopsy will more definitely establish the diagnosis.

DR. NELSON PAUL ANDERSON: I think psoriasis is a good working diagnosis. The eruption apparently clears spontaneously during part of the year and recurs during the rest of the year. This tends to make a diagnosis of dermatitis herpetiformis untenable. It might be worth while to test this man with the various pollens which are in season at the time of year when his eruption recurs.

DR. C. R. HALLORAN: I feel that the diagnosis in this case is psoriasis.

DR. A. F. HALL JR. (by invitation): The patient came to me with two letters, one of which was from Dr. M. F. Obermayer saying he should be relieved of all nervous strain and giving a diagnosis of dermatitis herpetiformis and the other from Dr. S. W. Becker, who did not vouchsafe a diagnosis but said that the patient should be relieved from emotional upset, hard work and nervous strain. I am particularly interested in getting some suggestions as to treatment. The patient says he has received a good deal of roentgen irradiation at various times and has had not the slightest benefit. A large amount of ultraviolet radiation was applied, and solution of potassium arsenite may have been used at the same time. Such therapy seemed to make no difference. The eruption has cleared up in early fall every year, either with or without treatment. I am at a loss as to how to give this man relief, for although he states that the itching is never severe, the eruption is unsightly and bothersome and predisposes to furuncles. The patient is rather uncooperative. He came here tonight only when told that he might get something that would cure him.

DR. MAX J. WOLFF: I should try administering calcium gluconate. I do not know of any specific treatment.

DR. A. F. HALL JR. (by invitation): The illogical thing about the story is that the condition is worse in the summer, but the patient came to California in the hope that the climate would do him some good. When I saw him I favored the diagnosis of atypical pustular psoriasis or possibly pityriasis lichenoides chronica.

DR. HARRY P. JACOBSON: I am not at all impressed with the diagnosis of dermatitis herpetiformis in this case. The patient presents none of the morphologic earmarks justifying this diagnosis. The condition, as I understand it, is of about fourteen years' duration—certainly a sufficient period for the lesions to show some suggestive confirmatory evidence of this diagnosis, such as pigmentation and scarring. Nor has pruritus been a prominent symptom. In view of all that, I am doubtful of the diagnosis as presented. However, for want of a better designation, I presume that label will do.

DR. SAMUEL AYRES JR.: I think that, irrespective of whether the disease is classified as psoriasis or dermatitis herpetiformis, the patient should have careful examination for focal infection. As far as treatment is concerned, it seems that nonspecific therapy, possibly administration of a little calcium thiosulfate and autohemotherapy, would be good in this type of case.

Tuberculosis Verrucosa Cutis. Presented by DR. NELSON PAUL ANDERSON.

A Case for Diagnosis (Xanthomatosis in Child? Recklinghausen's Disease in Mother? Recklinghausen's Disease [Forme Fruste] in Child?). Presented by DR. NELSON PAUL ANDERSON.

E. H., a white girl aged 3 years and 7 months, is an only child. Her mother has had Recklinghausen's disease for twenty-five years. This was aggravated by pregnancy. The patient presents typical café au lait areas on the upper inner parts of the thighs and on the abdomen. She also has pinpoint-sized yellowish xanthomatous lesions. About December 1934 the child sustained a pathologic fracture of the right leg, which has failed to heal after two and one-half years of treatment, including an open reduction.

DISCUSSION

DR. NELSON PAUL ANDERSON: These two patients are of interest because the mother presents well developed Recklinghausen's disease, while the child presents only the café au lait areas of pigmentation, without any sign of tumor formation. The child presents a nonuniting pathologic fracture of the tibia and the fibula of nearly three years' duration. Recently four or five pinhead-sized yellowish lesions have appeared on the abdomen. I wonder if any of the members feel that the pathologic fracture might be the result of xanthomatous lesions in the long bones,

which do occur. There are no bony defects in the skull, and there is no diabetes insipidus. There is, however, marked engorgement of the veins in both upper eyelids, which might be construed as part of an atypical Hand-Schüller-Christian syndrome.

Lichen Planus, Recurrent, with Extensive Oral Involvement. Presented by DR. PAUL D. FOSTER.

P. V., a middle-aged white man, a bakery distributor, presents a whitish eruption resembling a lace net which involves both sides of the mouth extensively, including the vermilion borders of the lips, especially at the angles of the mouth. On the legs and the arms are numerous flat-topped papules. On the left leg these papules have become coalescent to form a plaque. The patient is well nourished.

He has been given 2 cc. of mercury salicylarsenate intramuscularly every four days. There was marked relief after the sixth injection.

The patient had a similar eruption in 1933. Roentgen treatments then gave no relief. Many Wassermann tests and two tests of the spinal fluid in 1933 gave negative results. The eruption began on the legs three months ago and spread rapidly to its present general distribution.

DISCUSSION

DR. SAMUEL AYRES JR.: I think it would be justifiable to give up to fifteen or twenty injections of mercury salicylarsenate before making a change in therapy.

DR. H. C. L. LINDSAY: I have seen patients in whom lichen planus got a great deal worse under treatment with this preparation of mercury and arsenic and improved with injection of mercury bichloride. Arsenic aggravates lichen planus in some cases.

DR. KENDAL P. FROST: I think that in a case of this kind the oral lesions are a significant factor in prognosis. When oral lesions persist, the condition is prone to recur more frequently and more severely and to be more intractable to treatment than when there is no oral involvement.

Lichen Planus Sclerosus et Atrophicus. Presented by DR. KENDAL P. FROST.

G. D. B., a white man aged 43, an executive, presents on the front of the right upper quadrant of the chest, below the clavicle, a group of white sclerotic papules with brownish blue halos. On the lateral portion of the involved area is a group of purplish, streaky infiltrations. The duration of the lesions is about three years. They began as purplish spots and developed slowly. The first lesions turned white at the center as they became older. New lesions appeared gradually. There was no subjective sensation. The general appearance is good.

Histologic examination showed the epidermis to be narrow throughout. In one position there was slight hyperkeratosis, below which the outer portion of the corium was somewhat edematous and sparsely infiltrated with round cells. Deeper within the corium there were collections of round cells in the perivascular spaces. The diagnosis, made by Dr. E. M. Butt, was lichen planus atrophicus.

The patient was given five roentgen treatments of 80 r each, unfiltered, and 1/10 grain (0.006 Gm.) of mercury biniodide three times daily for six weeks. The entire period of treatment extended from Oct 14 to Dec. 4, 1936. In the wound resulting from removal of the biopsy specimen a small keloid developed. Two roentgen treatments were administered to that lesion, in January and in March 1937. The lesions have all lost the inflammatory element, and sclerotic scars alone remain.

DISCUSSION

DR. STANLEY CHAMBERS: The histologic picture seems most compatible with the diagnosis of the presenter.

DR. NELSON PAUL ANDERSON: The appeaerance of the sections might be more compatible with atrophic lichen planus than with lichen planus sclerosus et atrophicus. It is always dangerous to make such statements as this without

having observed the condition in its active stage. However, my idea of the latter disease is that there are practically always comedones in the central part of the lesions, and if these do not exist, I should hesitate to accept that diagnosis.

A Case for Diagnosis (Psoriasis?) Erythroderma [Toxic]?). Presented by Dr. Samuel Ayres Jr.

Miss M. Z., a white girl of 15, presents an eruption which began three years ago on the palms and later appeared elsewhere. It improves at times but never entirely disappears. The eruption is limited to the elbows, the knees, the ankles, the palms and the soles and extends dorsally on the fingers. The skin of the palms and the soles is diffusely red, with slight fissuring and superficial scaling. On the elbows and the knees and over the malleoli of the ankles are ill defined areas of redness and rather scant flaky scaling, which on the elbows have an almost lichenoid appearance. The scalp is uninvolved. The general appearance is good. The patient's mother had tuberculosis three years ago; one uncle had asthma. There has been no psoriasis in the family.

DISCUSSION

Dr. Samuel Ayres Jr.: This patient was seen for the first time yesterday. I should consider atypical psoriasis as a last resort. There is something peculiar about the distribution and the marked involvement of the entire palmar and plantar surfaces, with a slight amount of scaling. While there are lesions on the elbows and the knees, they are not, to my mind, clinically psoriatic lesions. The scaling is scant and on the elbows has almost a lichenoid appearance. There are a number of diseases besides psoriasis, such as gout and xanthoma, in which lesions occur over bony prominences. The distribution of these lesions is one argument in favor of psoriasis. I have not been able to bring out anything in the history which would suggest any toxic process. The total absence of lesions on the scalp is against a diagnosis of psoriasis.

Dr. H. C. L. Lindsay: This patient has definite pernio on the feet and a lichenoid rash with a psoriatic type of distribution.

Alopecia Areata Due to Arsenic and Arsenical Dermatitis. Presented by Dr. Irving R. Bancroft.

C., a man aged 32, a floor polisher, presents alopecia and itching dermatitis. He had a chancre at the urethral orifice in June 1936, two months after a cystoscope had been passed. The patient has been married for sixteen years and has had no extramarital intercourse. He was given neoarsphenamine until December, when its administration was stopped because of dermatitis. The alopecia began six weeks ago, and the hair is still falling out.

DISCUSSION

Dr. Irving R. Bancroft: I think that this condition is due to the toxic effect of arsenic on the sympathetic nerves.

Dr. Kendal P. Frost: Although the alopecia is in some respects patchy it is not as sharply limited as in definite alopecia areata. It seems to me to be a toxic type of alopecia. I do not recognize any type of alopecia peculiar to arsenic.

Dr. Irving R. Bancroft: I disagree with Dr. Frost, as the patient has not had dermatitis exfoliativa at any time.

Poikiloderma Atrophicans Vasculare. Presented by Dr. Irving R. Bancroft.

C., an Italian woman aged 49, who does housework for a living, presents a scaly erythematous rash all over her body, associated with some atrophy and varicose veins. There is marked exudation in places. A few places show practically normal skin.

DISCUSSION

Dr. Samuel Ayres Jr.: I thought of poikiloderma. There is atrophy over the breasts—a sort of telangiectasia, which strongly suggests chronic atrophy induced

by roentgen rays. As nearly as can be determined, no irradiation was ever given, but certainly there are vascular changes over the breast that would be consistent with leukoderma or with roentgen dermatitis.

DR. NELSON PAUL ANDERSON: I do not think Dr. Bancroft's diagnosis of poikiloderma should be taken too lightly, in view of the fact that the members agreed on this diagnosis four years ago. In many cases which are followed poikiloderma eventually turns into one of the lymphoblastomas. I can well believe that this condition is an exfoliative dermatitis that represents the end-stage of poikiloderma or the beginning stage of one of the lymphoblastomas affecting the skin.

DR. L. F. X. WILHELM: I think the possibility of lymphoblastoma has to be ruled out.

DR. IRVING R. BANCROFT: The patient was seen here about four years ago. At that time the members agreed on the diagnosis. The condition appears to be growing worse. It has lasted twenty-three years and has not changed much lately.

Granuloma Coccidioidale. Presented by DR. HARRY P. JACOBSON.

E. G., a youth aged 18, entered the Los Angeles County Hospital last fall because of a peritonsillar abscess which discharged a good deal of pus and which on microscopic and cultural study showed characteristic coccidioides immitis. The peritonsillar abscess was traceable to lymph nodes in the anterior triangle of the neck, which, in turn, drained one or two cutaneous lesions in that neighborhood. Coccidioides vaccine was administered, and there was marked improvement in a short time. The improvement was so marked that the patient decided to leave the hospital and disappeared from view for almost three months. In the middle of March he reappeared, showing extensive involvement of the left sternoclavicular region, together with involvement of all the soft tissues and the overlying skin in that area. I am presenting him to show the results of vaccine therapy. I desire to direct special attention to the comparatively brief time since vaccine therapy was resumed and the degree to which the involvement has receded.

Granuloma Coccidioidale. Presented by DR. HARRY P. JACOBSON.

S. L., a youth aged 18, came under my care in May 1934, suffering from destructive bony involvement of the clavicles, together with some abscess formation in the overlying soft tissues of the left clavicular region. To the best of my recollection, there was roentgenologic evidence of pulmonary involvement at the time. The patient gave a history of injury to the left leg in the course of his employment and stated that the present trouble was a result of that injury.

I am presentnig this patient to show the results of therapy. For about two years I used my usual injections of colloidal copper plus injections of coccidioidin. The response was satisfactory to a degree; however, the patient remained an invalid and was unable to resume his normal occupation. In September 1936, I commenced treatment with my new coccidioides vaccine. The results of that new treatment speak for themselves. The patient has for some time past been engaged in his usual occupation, putting in a full day's work every day. In October a cold developed which partially incapacitated him for a few days. A few weeks ago pain developed in the left shoulder. This was traced to an extensive dental infection. Since the elimination of that infection, the pain in the shoulder has largely subsided.

Granuloma Coccidioidale. Presented by DR. HARRY P. JACOBSON.

E. C., a boy aged 6 years, is presented to show the therapeutic efficacy of injections of colloidal copper and coccidioidin. When he came to my service at the Los Angeles General Hospital he was about 3 years old. When first seen he presented an involvement of the right side of the chest wall, associated with an intrapleural involvement. The clinical history of the condition dated back some months at the time of the first examination. I am unable to recall the exact

history, for I have not the chart from the Southwest General Hospital before me. To the best of my recollection, colloidal copper has not been administered for almost a year. To all appearances, his condition is satisfactory.

DISCUSSION

DR. SAMUEL AYRES JR: I think that Dr. Jacobson is to be highly congratulated on the excellent results of treatment of this almost uniformly fatal disease. It is a rare treat to see these three patients in whom coccidioidal granuloma is in a quiescent stage, some of whom have had intrathoracic lesions. Dr. Jacobson deserves the congratulations of the members on the method of treatment he has devised for this otherwise hopeless condition.

DR. H. C. L. LINDSAY: Thirty-five years ago some of these cases of granuloma coccidioidale would have been diagnosed as instances of tuberculosis of the skin. Today they probably would be diagnosed the same in their early stages, if it were not for the microscopic picture.

DR. C. R. ANDERSON: What is coccidioidin?

DR. HARRY P. JACOBSON: Coccidioidin is a filtrate of endotoxin and exotoxin. The nature and the method of preparation of the exotoxin I described several years ago (ARCH. DERMAT. & SYPH. **21**:790 [May] 1930). Its chief use is in diagnosis. If it is injected cutaneously in the presence of coccidioidal infection, a specific cutaneous allergic reaction results. For therapeutic purposes, however, I am not employing coccidioidin any longer, for I have an antigenic vaccine which contains all the components of the coccidioides. I have about ten or eleven patients with granuloma coccidioidale under my care now. The treatment given is limited to coccidioides vaccine and halibut liver oil by mouth. Except in the acute fulminating type of granuloma coccidioidale accompanied with meningeal involvement, I feel justified in saying that the prognosis is good in most of the cases in which this treatment is used.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

J. GARDNER HOPKINS, M.D., *Chairman*

May 4, 1937

DAVID BLOOM, M.D., *Secretary*

Lupus Miliaris Disseminatus Faciei. Presented by DR. ABRAHAM WALZER, Brooklyn.

A. B., a woman aged 52, is presented because of an eruption on the face of four years' duration. There is nothing in her past history of any importance and no history of tuberculosis in the family. The lesions involve practically the entire face and occur as discrete and grouped millet-sized soft elevated brownish red papules. Some of them show a slight central softness or flattening, and some present a faint surrounding erythema. On diascopic pressure they appear apple jelly colored. Intermingled with these papules are tiny brown depressed scars, the remains of former lesions. Some of them show a surrounding areola, and some do not. The lesions occur in crops and have no tendency to enlarge.

Roentgenograms of the chest showed no evidence of tuberculosis. The histologic observations were those of tuberculosis of the skin, with tubercles limited chiefly to the cutis. Tuberculin tests with dilutions of 1 : 10,000 and 1 : 1,000,000 were performed in April 1936, but the results could not be read. Previous to the tests the patient had had a fungous infection of the hands for about six weeks, and at the time of the tuberculin tests she showed a fairly marked vesicular fungous eruption of both hands. Two days after the injections of tuberculin the

upper extremities became swollen and erythematous and masked the sites of the tuberculin tests. Erythematous patches appeared on the chest, the neck, the trunk and even the thighs. This condition lasted for about ten weeks and was followed by exfoliation.

DISCUSSION

DR. ABRAHAM WALZER, Brooklyn: The question is whether the reaction subsequent to the injection of tuberculin was due to a lighting up of a tuberculous focus somewhere in the system or whether it was a nonspecific reaction resulting from a stimulation of the dermatophytosis of her hands. If it had been a lighting up of a tuberculous focus, the patient would have been a sick woman; as a matter of fact, she was not. I believe that the condition was a dermatophytid resulting from a nonspecific stimulation of the dermatophytosis of her hands.

A Case for Diagnosis (Scrofuloderma?). Presented by DR. ABRAHAM WALZER, Brooklyn.

N. LaC., a boy aged 12, has been presented previously on three different occasions. The first presentation was before this section on May 2, 1933, when there was a diagnosis of erythema multiforme haemorrhagicum bullosum (ARCH. DERMAT. & SYPH. **28**:894 [Dec.] 1933); the second, before this section on Jan. 2, 1934, when there was a diagnosis of disseminated lupus erythematosus with pernio (ARCH. DERMAT. & SYPH. **30**:145 [July] 1934), and the third, at a clinical meeting of the American Dermatological Association on June 9, 1934, when the diagnosis was granuloma annulare (?) or sarcoid (?) (ARCH. DERMAT. & SYPH. **30**: 867 [Dec.] 1934).

DISCUSSION

DR. ABRAHAM WALZER, Brooklyn: On the first presentation of this case by Dr. Goodman, in 1933, the diagnosis of erythema multiforme bullosum haemorrhagicum was accepted by some of the members, while others suggested Duhring's disease and urticaria pigmentosa. When I presented the case as one of disseminated lupus erythematosus with pernio, six months later, other diagnoses suggested were erythema multiforme, granuloma annulare, sarcoid and epidermolysis bullosa. Six months later, Dr. Rosen presented this case as a case for diagnosis, with tentative diagnoses of granuloma annulare and sarcoid. In the discussion that followed it was brought out that on histologic examination of tissue removed from a nodule, from a lesion on the buttocks, and from the ear a diagnosis could not be made, but only a suggestion of granuloma annulare was possible. This presentation of the case is the fourth one, and the lesions are different from any previously seen. Clinically, the lesions, on the face and the ears especially, are suggestive of tuberculosis. The case is presented for diagnosis.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I should make a diagnosis of lupus pernio.

DR. LOUIS CHARGIN: I have had occasion to study this patient for an extended period in the Mount Sinai Hospital in the service of Dr. Isadore Rosen, and I believe that I have established a diagnosis. None of the various diagnoses suggested appears to be correct. The diagnosis was missed because sections of the tissues, examined by others, did not include stains for fat. I believe this patient is suffering from a lipoid disturbance of the skin. It appears to be the first example of this particular type of lipoid disturbance that has been presented in this city. The case reported by Dr. R. N. Tripp (*N. Y. State J. Med.* **36**:619, 1936) differs somewhat from the case in question, in that the disturbance in the fat metabolism in Dr. Tripp's case was of lipoid protein and that in this case is of cholesterol ester origin.

The lipoidoses, considered from the chemical standpoint, may be roughly divided into perhaps four groups: (1) those that show the cholesterol inside the cells, the so-called foam cells; (2) those in which the cholesterol and the ester are extracellular (Kerl and Urbach); (3) those in which the fat is a phosphatide, as in Niemann-Pick lipoidosis; (4) those in which the fat is in combination with

the protein (Urbach and Wiethe). Those in which cerosin is present are of still another type. In the case presented this evening the fat is cholesterol and ester and is intracellular, but clinically the case resembles that reported by Dr. Tripp, except that this patient never showed any manifestations in the throat and little eruption that can be regarded as characteristic of this disease (Urbach and Wiethe) in the mouth. In other words, while the eruption is not unlike that in Dr. Tripp's case, the fat concerned is different.

DR. HERMAN GOODMAN: I saw this child years ago and was unable to make a clinical diagnosis but depended on several histologic specimens on which a diagnosis of erythema multiforme bullosum haemorrhagicum was made by Dr. E. A. Barthel. The case was presented with that diagnosis. The boy does not look any different tonight from the way he did several years ago. When I saw him again tonight, the diagnosis of lipoid disturbance occurred to me. I was reminded of the cases of two girls who were presented many years ago with the diagnosis of Hutchinson's eruption and have since been studied and reported as instances of lipoid-protein disturbance. In neither case were there any such lesions as this boy shows. Whether Dr. Chargin can link the conditions all together or not I do not know.

DR. ISADORE ROSEN: I do not know if Dr. Goodman remembers this case well when he says it presents tonight the same features it did when he reported it (*Arch. Pediat.* **53**:676, 1936). At that time there were large bullous and hemorrhagic lesions, which are not evident now. At that time every one agreed with the diagnosis of bullous hemorrhagic erythema multiforme. The type of lesion which the patient shows tonight is more or less fixed.

As Dr. Chargin said, the boy was in my service at the Mount Sinai Hospital for at least six months, and all types of investigation were carried out. One of the interesting findings was a marked reduction in the total cholesterol of the blood, which was found to be 100 mg. per hundred cubic centimeters, consisting of 50 mg. of cholesterol esters and 50 mg. of free cholesterol. This finding may coincide with the diagnosis that Dr. Chargin suggested in this case, of a marked disturbance in the lipids of the skin.

DR. FRED WISE: Dr. Chargin's remarks interested me because two sisters afflicted with lipoidosis cutis et mucosae are at present under the care of Dr. C. R. Rein and me at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. Both girls have prominent lesions in the upper part of the respiratory tract, in the mouth and on the lips, and both are hoarse. The diagnosis of lipoidosis cutis et mucosae would be untenable for a patient who was not hoarse and who had no buccal manifestations of the disease.

DR. GEORGE C. ANDREWS: If this condition is called extracellular cholesterosis, how can there be foam cells? In that disease the cholesterol is extracellular. I do not recollect the description of any bullae or ulcerative lesions in extracellular cholesterosis. Instead, there are nodules and tumor formations. I should like to know more about Dr. Chargin's reasons for making the diagnosis.

DR. LOUIS CHARGIN: In the hospital it was possible to observe the development of the lesions in this case from start to termination. The primary lesion was a small papule, which spread at the periphery and soon became capped with a vesicle. As the lesions grew larger, they assumed the characteristics of erythema multiforme. In the course of time the lesions disappeared, some of them leaving no trace and others leaving superficial or deep scars. Still others remained nodular. New lesions continually appeared in new sites and in the scarred areas. Apparently the lesions itched a good deal, since the child scratched constantly. As a result of the scratching an infection developed in the leg, and there was high temperature. During the period of infection it was interesting to observe that many of the lesions disappeared, only to reappear when the infection subsided. While the patient was in the hospital, severe herpes zoster developed on one leg. This, too, was accompanied by a high temperature. All types of treatment were tried—insulin therapy, a low fat diet and a low sugar diet—none of which had much influence on the course of the disease. The cholesterol content of the blood

varied considerably from time to time but was never high. This feature has been reported in other cases. The process is a disturbance of fat metabolism, of which the principal part takes place within the skin.

DR. E. WILLIAM ABRAMOWITZ: Dr. Chargin's report of this case is interesting to me. I remember the patient well, as he was under treatment at the New York Post-Graduate Medical School and Hospital six or seven years ago. The histologic examination showed possible granuloma annulare, but my associates and I were not satisfied with that diagnosis. After studying the case for about six months, I suggested the possibility that the condition was some form of lipoidosis. Lipoid studies were started just before the boy disappeared from observation.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I think the lesion on the ear is certainly suggestive of lupus pernio and that this diagnosis still may be close to the correct one.

DR. J. GARDNER HOPKINS: When one studies lipoid deposits in this disease, it is so easy to assume that when lipoid is found the condition has been explained. I think that the more types of lesions are examined for lipoid, the more will be found in which there are lipoid deposits. I am much interested in Dr. Chargin's remarks. At the same time, I think a little reserve is advisable in assuming that once lipoid has been found in a lesion the lesion has been explained.

DR. ABRAHAM WALZER, Brooklyn: I should like to say a few words about lipoids in the blood. Up to the present time the only type of metabolic lipoid disturbance of the skin about which anything was known was xanthoma. Recently there has been a further development in the study of lipoids, and there are now recognized dermatologic conditions due to phospholipids, to galactolipids and possibly to others. The galactolipids include the lipoproteins.

The quantity of free or combined cholesterol in the blood is not the only essential fact in an explanation of xanthoma. In about 30 per cent of cases of xanthoma there is a normal or even a deficient cholesterol content. Nevertheless, there are deposits of cholesterol in the skin in these cases. In other words, the conception at present is that the absolute quantity of cholesterol is not so important as the amount of cholesterol in relation to the quantities of other lipoids in the blood. When the normal quantitative relation of one fat to the other is interfered with, there is a precipitation of one or more of these lipoids and a deposit of the lipoids in the skin or in other organs.

Within recent years Urbach and his associates have reported a series of cases in which another lipoid, lipoid-protein, was deposited in the skin and the mucous membranes. Every one of these patients was hoarse because of involvement of the larynx. Lesions were found in the mouth. On the body the lesions were nodular and resembled papulonecrotic tuberculids.

In the case presented tonight, while it is in all probability true, as stated by Dr. Chargin, that the boy does show some lipoid changes in the skin, no changes in the ratios of the lipoids in the blood or in the skin have been shown. Nothing but cholesterol is reported on. As Dr. Hopkins has remarked, I think a little slow going is in order before the conclusion is accepted that this case is one of lipoid disturbance merely because a lipoid has been demonstrated in the skin. More quantitative as well as proportional studies in the lipoids in both the skin and the tissues must be made before this case can be called one of lipoid metabolic disease.

Clinically, the condition looks like tuberculosis of the skin. On the other hand, Dr. Chargin's finding of increased cholesterol in the skin might apply; but in addition is it not still possible that the destructive lesions on the skin are induced by the tubercle bacillus? In other words, the lesions are tuberculosis on a skin containing excessive lipoid.

A Case for Diagnosis (Pyoderma Gangraenosum?). Presented by Dr. HERMAN GOODMAN and DR. LUDWIG OULMANN.

Mrs. A. P., a woman aged 61, a patient of Dr. M. W. Buchbinder, of Jamaica, N. Y., had no cutaneous lesions before April 6, 1937. Since that date lesions have

developed and have become gangrenous in large areas on both arms and have receded on one knee and one flank and over the left scapula. The lesions began as small ecchymotic spots. Edema developed, and the lesions appeared telangiectatic, infiltrated and pigmented. There was a hard covering resembling a turtle-shell in some areas, and beneath it was ulceration. All this developed within a few days. The patient's temperature ran from 101 to 102 F. Areas on the flank and one knee and over the left scapula have cleared entirely. The lesions on the arms have sloughed. Photographs showing the lesions before sloughing occurred are presented. The patient has hypertension.

The blood count showed 3,890,000 red blood cells, 72 per cent hemoglobin, a color index of 0.94, 8,350 white blood cells, 58 per cent polymorphonuclear leukocytes, 35 per cent lymphocytes, 4 per cent monocytes, 3 per cent eosinophils, 132,160 platelets and slight polychromia. The bleeding time was three minutes and the coagulation time five and one-half minutes. Examination of the urine showed a specific gravity of 1.005, a 2 plus reaction for albumin, 6 white blood cells per high power field, small clumps of pus and no casts. The Wassermann reaction of the blood was 4 plus. The Wassermann test of the husband's blood was negative on several occasions. Examination of a histologic specimen showed nothing pathognomonic in the sections, which were stained in many ways. Dr. Machacek reported that "one must consider that the vascular changes are possibly due to the syphilitic infection."

Dr. Buchbinder has initiated a course of antisyphilitic treatment.

NOTE.—On Jan. 10, 1938, Dr. Buchbinder reported that the lesions of the arms had healed completely under antisyphilitic treatment. The patient left the city for the summer and returned with a gumma, which led to perforation at the saddle of the nose. She had been bedridden with bronchitis on two occasions when she was to have been presented. Histologic and therapeutic evidence leaves no question regarding the syphilitic nature of the unusual lesions of the skin.

DISCUSSION

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I should think first of a metabolic disturbance, particularly of diabetes, which would explain the ecchymosis and the necrosis; second, of a vitamin deficiency, and third, of a late type of malignant syphilis. If the lesions should not respond to antisyphilitic treatment, this would not speak against syphilis; on the other hand, if all antisyphilitic treatment should fail, avitaminosis should be considered. As far as the histologic picture is concerned, one would not expect to find a typical picture of syphilis, and its absence would not speak against the diagnosis of syphilis.

DR. E. WILLIAM ABRAMOWITZ: While I have not seen the telangiectasis and ecchymosis, the spread of the lesion reminds me much of pyoderma grangraenosum. In fact, there is a patient in the hospital now with an extensive ulceration of one leg closely resembling ulcerating syphilis. Antisyphilitic treatment caused no improvement. The patient is just about holding her own after two blood transfusions, which seemed to be of help. I favor the diagnosis of pyoderma gangraenosum.

DR. LOUIS TULIPAN: There are two things to be considered here: In the first place there is the possibility of an embolus, similar to that in a case under observation at the Bellevue Hospital last year. The patient had had an injection in the buttock of a bismuth preparation, and an embolus was produced, followed by gangrene, complete destruction of the deep tissues and ulceration almost like this. The other thing to consider here is a factitious lesion. A condition of this kind might be due to the application of phenol and be followed by gangrene. I feel that if this condition were due to syphilis there would not be such deep destruction of tissue in three weeks. It would take many months for a lesion like this to develop. I cannot conceive of anything like this occurring in syphilis or in diabetes in so short a time. Therefore, I believe the two conditions I mentioned should be considered.

DR. DAVID BLOOM: I agree with the diagnosis of gangrenous pyoderma. I have observed a number of cases in which gangrene of the skin developed rapidly, preceded by bluish discoloration of the skin. In fact, I was able to reproduce the rapid development of gangrene of the skin by injecting a mixture of the microorganisms of one patient into the skin of rabbits. Syphilis, tuberculosis, colitis or arteriosclerosis may be the underlying weakening factor. I have observed such associations in cases at the Bellevue Hospital and in two cases which I have observed together with Dr. Abramowitz.

DR. CHARLES WOLF: This condition is a type of ecthyma térébrant. The destruction of tissue is marked. The disease generally occurs, however, in younger people, cachectic children particularly.

DR. GEORGE C. ANDREWS: I agree with Dr. Bloom's diagnosis of ulcerative pyoderma, with syphilis as the predisposing cause. I might add to his remarks that if amebas are not recovered, the treatment recommended by Dr. F. L. Meleney of dressings of zinc peroxide might be of benefit.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I had not understood that the condition had developed so recently, but since the patient has an elevation of temperature, I think the possibility of gangrenous erysipelas should be considered.

DR. SIGMUND POLLITZER: I cannot reconcile the lesions presented in this case with any of the diagnoses suggested except one. Unreasonable as it may appear, I venture to suggest that these remarkable lesions are self-inflicted—are artefacts—and I should like to suggest that a further study of the case be made with that possibility in mind.

DR. EDWARD R. MALONEY: I should like to agree with Dr. Pollitzer that the lesions are artefacts.

Effect of Sun: Fixed Eruption in Sunburned Areas of Skin After Ingestion of Phenobarbital and During Medication with Arsphenamine. Presented by DR. HERMAN GOODMAN.

Mrs. J. S., a woman aged 34, born in Germany, presents an eruption on those areas of her trunk which were exposed when she wore a modern halter top bathing suit. The eruption consists of reticulation and, in a few areas, of wart formation. The patient's face, which was always covered by a layer of cream and powder during exposure, does not show the eruption. The limbs are practically clear, except for the feet, because the patient kept them covered. She never went into the water, although she was on the beach every day of the summer. In filtered ultraviolet or black light, the lesions present an appearance similar to that of lentigo under this form of illumination, and there is a suggestion of a similar eruption on the inner aspects of the thighs.

The patient took phenobarbital in large doses in the summer of 1936 and was exposed to the sun under the following conditions: She used a mask of cream covered with powder for her face and wore a halter top bathing suit and slacks. In the fall of 1936 the skin was perfectly normal, and she had no lesions of any kind. She read about the effects of syphilis in the newspapers and went to a physician. The Wassermann test of the blood was negative, but ten injections of arsphenamine were given. At the end of this series her skin presented an eruption on the sites where she had been previously sunburned.

A chronological review shows the following sequence of events: The patient took phenobarbital from August 1935 through the fall of 1936. She was exposed to the sun in the summer of 1936. Arsphenamine and a bismuth preparation were given in the fall of 1936. The eruption appeared after the tenth injection of arsphenamine. It lessened somewhat after she ceased taking phenobarbital, although treatment with arsphenamine and the bismuth preparation was continued. The eruption followed the outline of the skin which had been exposed to the sun.

DISCUSSION

PROF. A. BUSCHKE, Berlin, Germany (by invitation): At first glance one would not suspect an arsphenamine eruption of any kind. The only eruption due to arsphenamine that might give a similar distribution is the lichenoid type. I have never seen atrophy following the use of arsphenamine. This patient demonstrates superficial atrophy in the previously affected areas. I think the condition is possibly a syphilitic exanthematous eruption localized in this form and leaving atrophy.

DR. FRANK C. COMBES: I think this patient has a condition which, if not the same, is at any rate related to poikiloderma of Civatte. Riehl described this condition. He considered it due to coal tar or products of coal tar. Later Civatte independently described the same complex and stated that in some cases the condition was not due to coal tar and that exposure to the sun could produce the lesions in some patients.

DR. E. WILLIAM ABRAMOWITZ: I agree with Dr. Combes. If I did not know anything about the history here, I should make a diagnosis of poikiloderma of Civatte. The fact that the barbiturates will sensitize the skin to sunlight may have some significance in this case. This eruption is not of fixed type, as there has been no recurrence in situ. There are several types of eruption which are apt to locate on a sunburned area, one of them being lupus erythematosus, and this disease should be considered.

DR. EUGENE F. TRAUB: I agree with the diagnosis Dr. Goodman presented. According to the original description, typical poikiloderma of Civatte does not take in so much territory as this eruption, which is present on the forearms and the arms, certainly not typical locations for poikiloderma of Civatte. On the other hand, I can see no reason why the condition cannot be considered a typical arsphenamine eruption in a patient who is sensitized on certain areas by sunburn and previous medication, the sunburn predisposing the location of the eruption to these areas. Some months ago I presented before this section a patient with arsphenamine dermatitis showing exactly this clinical picture (ARCH. DERMAT. & SYPH. **36**:194 [July] 1937). The lesions, too, were annular papules resembling lichen planus, with pigmentation and atrophy, and I believe that picture is typical at times of an arsphenamine eruption.

DR. HERMAN GOODMAN: I want to point out that the physician continued to give arsphenamine after the eruption appeared, and there was no exacerbation; and that when he learned that the patient was still taking phenobarbital he ordered that discontinued, and the eruption improved. There have been eruptions on sunburned skin due to phenobarbital and eruptions on sunburned skin due to arsphenamine. This patient had no eruption due to phenobarbital, but the arsphenamine caused the eruption on the parts which had been previously exposed to the sun. I have not observed this association before.

Poikiloderma Atrophicans Vasculare. Presented by DR. OSCAR L. LEVIN.

C. S., a boy aged 10 years, born in Italy, suffers from a generalized condition of the skin which first appeared when he was 2 years of age. It was first confined to the face and the hands. From the face it spread gradually to involve the neck and the trunk. During the past year the eruption has become more marked and has spread over various parts of the trunk and the extremities. He has always been well except for coldness of the hands and the feet. A recent general examination revealed nothing abnormal except the presence of the eruption and cardiac irregularity. His family history is irrelevant except that his mother is suffering from hay fever and asthma.

The examination of the skin discloses a generalized eruption, most evident on the face, the neck, the upper part of the back and the extremities. The face shows a diffuse irregular reticulated brownish pigmentary condition, and scattered over the chest there are numerous small and large telangiectases. These are discrete linear dark red lesions and show scattered small ring formations of the vessels.

Brownish pigmentation occurs in large macules on the trunk, particularly on the upper part of the back and the neck. The skin of the hands and the feet is purplish and presents small hemorrhagic spots. There are numerous telangiectases and superficial spots of atrophy, with a purplish discoloration of the skin over the front part of each knee. On these sites there are numerous pinhead-sized, slightly elevated, shiny papules. Small areas of atrophy are present on the face. Associated with these lesions, dermographism and transient patches of erythema are marked on the front of the trunk. The skin of the hands and the feet feels cold and deeper palpation shows the backs of the hands and the feet to be infiltrated, suggesting beginning scleroderma. The mucous membranes are normal.

DISCUSSION

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I think this case requires a great deal of observation, but from what can be seen tonight I should be inclined to consider it one of vasomotor neurosis of the skin. There is no atrophy. The differences in color are due to differences in filling of the blood vessels rather than to atrophy of the skin. There is dermographia, which would fit in with vasomotor neurosis.

DR. FRED WISE: My first impression when I looked at this condition was of a nevus or a nevoid disease, but with the clinical symptoms which Dr. Levin has so well described—that is, the sclerodermic skin, which I did not have the opportunity to observe, telangiectasia and changes which somewhat resemble dermatitis due to roentgen rays—his diagnosis of beginning poikiloderma atrophicans vasculare must be seriously considered. I was unable to detect the various changes he noted, but he has had the advantage of seeing the patient in daylight and over a longer period than the members have.

DR. EUGENE TRAUGOTT BERNSTEIN: Cassirer in his classic work on trophoneuroses (Die vasomotorisch-tropischen Neurosen, Berlin, S. Karger, 1901) emphasized that scleroderma, sclerodactylia, acro-asphyxia, acrocyanosis and other vascular disturbances, as well as changes in pigment and atrophy, may occur simultaneously. This patient presents such a combination. There are definite symptoms, such as beginning atrophy, vasomotor changes and pigmentary displacement. I agree with Professor Buschke that a vasomotor neurosis is probably responsible for the previously mentioned changes, and, in my opinion, pigmentary disturbances should be considered trophodermatoses.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): A case of poikiloderma of eight years' duration should show definite atrophy. Since this is not present and the difference in color has a parallel in the presence of changes resembling naevus anemicus and a telangiectatic nevus, I should say that the presence of hyperemia and white discoloration is due to vasomotor changes. I think the pigmentary change is the result of healing of some previously hyperemic areas rather than of a disease of the pigmentary system itself.

DR. EUGENE F. TRAUB: I should like to express agreement with the last speaker, because I do not believe the discoloration on the face is due to a pigmentary change at all. It is all part of a vascular process. In some areas the skin is simply deeper red than normal, owing to an increased vascularity, giving the impression in this light of a deeper brown. The lighter areas are blanched and by contrast appear depigmented. As Professor Buschke has said, the condition is a naevus anemicus, associated with a vascular nevus of the naevus flammeus type.

DR. OSCAR L. LEVIN: There is definite pigmentation in widespread areas, and the patient shows distinct evidences of vasomotor disturbance. Associated with this, there are marked telangiectatic formations, atrophy and a tendency to beginning scleroderma. The child was not brought back to the office for further study, because the mother was ill with pneumonia. I believe the whole condition is due to an endocrine disorder.

Pityriasis Lichenoides et Varioliformis Acuta. Presented by DR. ABRAHAM WALZER, Brooklyn.

S. W., a man aged 20, is presented because of an eruption on the trunk and the extremities of three weeks' duration. The patient has never had any serious illnesses. The present trouble began on the upper part of the trunk and spread to its present locations. There has been slight itching.

The eruption consists of macules varying from red to yellowish red and slightly elevated papules. The lesions vary in size from that of a pinhead to that of a pea. Some have a shiny, almost violaceous aspect; others are covered with a fine scale. Some are surmounted by a hemorrhagic crust and have the appearance of varicella. The eruption is symmetrical. The external glands are not palpable. There are no lesions in the mouth, and the patient does not feel ill.

DISCUSSION

PROF. A. BUSCHKE, Berlin, Germany (by invitation): Cases like this are rather rare in Germany, and they gave considerable difficulty in diagnosis until the Viennese papers on the subject appeared. Even so, there is some doubt whether this condition really belongs to the group of parapsoriasis, although I am willing to accept that diagnosis.

DR. PAUL GROSS: The interesting feature here is the close resemblance to pityriasis rosea, if the most exudative lesions are disregarded. I remember the discussions in the literature when the first cases of acute parapsoriasis were presented in London. Some dermatologists were so impressed with this resemblance that they even considered a relation to pityriasis rosea. I agree with the diagnosis as presented, and suggest a biopsy.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I absolutely disagree with the possibility of pityriasis rosea here. While there are sometimes exudative lesions in pityriasis rosea, there are along with these, typical lesions of pityriasis rosea.

DR. PAUL E. BECHET: In my opinion, some of the puzzling features of this case are probably due to the recent development of the eruption. If I remember correctly, it is only two or three weeks old. When this is taken into consideration, the case still presents features that are fairly typical. There are many features of a varioliform eruption, as well as papules and slightly scaly patches. A few weeks ago there was a case at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, which presented all the classic lesions of pityriasis lichenoides et varioliformis acuta, and there were vesicles and slightly scaly guttate lesions. I am under the impression that changes from the vesicular type to the typical guttate type, and vice versa, occasionally occur, and that the disease presents stages of remission, or even total disappearance, in contradistinction to ordinary parapsoriasis, which is usually persistently present.

DR. ABRAHAM WALZER, Brooklyn: The condition is of only three weeks' duration. More of the varioliform type of lesions have developed in the last day or two. Lesions resembling pityriasis rosea and even of similar distribution are described at the onset of this condition; so that does not mitigate against the diagnosis in this case.

Multiple Keloids. Presented by DR. ABRAHAM WALZER, Brooklyn.

M. S., a girl aged 18, is presented because of lesions on the sides of the face, the shoulders, the chest and the neck, of five years' duration. The patient had acne at the age of 10 years, and the first keloid appeared on the chest at the age of 12. About three years ago she received about ten treatments with roentgen rays to the face, the chest and the back. Two years ago the large lesion on the chest was treated by cautery in another institution, and the patient received about twenty-four intramuscular injections, the last one about four months ago. No benefit resulted. At the latter institution a histologic examination was done on a lesion

from the back. There was nothing else in the past history of any importance. The lesions have been constantly increasing in size and number.

In the upper part of the sternal region is a raised, almost palm-sized plaque, irregular shaped, crab like and with many variously shaped extensions radiating in different directions. The patch is flat, smooth, hard, violaceous and sharply outlined and has an almost perpendicular border. Surrounding it and scattered over the previously mentioned locations are many globular nodules, varying in size from that of a pea to that of a dime, and scattered, irregularly conglomerated or arranged in lines. They vary in color from red to brown to violet. Many of them show a combination of these colors, and others have a red or a pink center and a darker border. They are all smooth and hard and move with the skin. Itching is the only symptom. In addition to these lesions and intermingled with them are many soft flat pitted or wrinkled scars, pea-sized or a little larger, the remains of preceding acne. Scattered throughout, especially on the back, are many comedones, some of them within the keloids.

DISCUSSION

DR. PAUL E. BECHET: It is known that trauma plays just as important a role as predisposition in the production of keloids. Suspecting that the lesions had been caused by pinching and squeezing in an attempted relief of acne, I elicited from her the facts that she daily squeezed and pinched comedones and pustules on the chest and the face and that her sister did the same thing on the lesions on the back, which the patient could not reach. There is no doubt in my mind that self-inflicted trauma is the cause of the keloids in this particular case. The patient's predilection for keloids must be weak, as she has a large vaccinal cicatrix which is not in the least keloidal.

DR. FRED WISE: I should like to call attention to the statement of the patient that she received about a hundred injections of thiosinamine, which produced no effect. Some of the substance was injected into the keloid itself. I speak of this because in years of experience with this drug, I have not observed a single instance in which it had the slightest effect on a keloid when injected into the unaffected skin, and I think, therefore, that it should not be used for that purpose.

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I should consider the possibility here that not acne but some other type of infection is present. Bacteriologic studies are in order, so that at least the spread of the condition and the development of new keloids may be prevented by attempts at immunization. As far as treatment is concerned, I have had poor results with roentgen treatment of keloids and no results at all with fibrolysin. My best results have been with radium, but I cannot conceive of treating such an extensive involvement with radium. Radon has been used intravenously in the treatment of mycosis fungoides, and in a case like this that form of treatment might be employed, in order to affect the entire body with radium.

DR. DAVID BLOOM: At the Bellevue Hospital at present there is a similar case. A young girl presents on both shoulders keloids which developed following acne vulgaris. As the lesions did not respond to roentgen therapy, they are now being treated with solid carbon dioxide. I should like to hear the experience of the members with this type of treatment.

DR. FRANK C. COMBES: I wish to endorse what Dr. Bloom has said. I have had my best results in old keloid with solid carbon dioxide and subsequent treatment with radium. With properly administered radium the keloid completely disappears, without any danger of radiodermatitis. Of course, in a case like this, application of radium is simply impossible.

DR. ABRAHAM WALZER, Brooklyn: There has been a progressive increase in the lesions, without trauma or other apparent cause. The scars resulting from the acne are not keloidal but soft. The keloids, therefore, are independent of the acne. I cannot imagine a treatment involving trauma of some kind, whether roentgen or radium irradiation or medication with solid carbon dioxide or an

acid, that will be of benefit. First of all, there are entirely too many lesions to treat by such methods, and secondly, the end-result of the trauma will be more hypertrophic scars or keloids. This patient possesses some underlying predisposition to the formation of keloids, and I think, therefore, that the less traumatic therapy is given, the better for the patient.

Blastomycosis. Presented by DR. ANTHONY C. CIPOLLARO.

F. L., a man aged 28, born in the United States, a jeweler, has an eruption which began about eight months ago. At first the lesion had the appearance of a furuncle and became progressively worse in spite of various topical remedies which were prescribed by his family physician.

The patient presents an oval lesion measuring approximately 3 by 1½ inches (7.5 by 4 cm.) on the left side of the chest just below the clavicle. The lesion appears to be made up of many tiny sinuses, from which great quantities of yellow pus can be expressed easily. The margin is infiltrated and sharply demarcated. There is a similar lesion over the right scapula about the size of a dime.

Smears showed Blastomyces dermatitidis in great numbers. The pus was cultured, but up to the present time nothing has grown. Roentgenograms of the lungs will be taken within the next day or two. The histologic picture confirmed the diagnosis of blastomycosis. The epidermis showed marked irregular acanthosis and was covered with a crust, made up of fluid and detritus. The abscesses in the epidermis were full of polymorphonuclear leukocytes. In the subepidermal zone and to a lesser degree in the deeper parts of the cutis there was a diffuse infiltrate made up mostly of plasma cells and connective tissue cells and containing some polymorphonuclear leukocytes. There were dilatation of the vessels and considerable edema.

DISCUSSION

PROF. A. BUSCHKE, Berlin, Germany (by invitation): I have never seen the condition in such an early stage, although I am familiar with the fully developed type of malignant blastomycosis described by Montgomery. The fact that so far nothing has grown on culture speaks against the European type of the disease, which also has a different clinical picture, with gumma-like lesions which break down rapidly and extrude their contents. I am grateful for the opportunity of seeing such an early involvement.

DR. J. GARDNER HOPKINS: I think this is an interesting case. There is less verrucous development than there has been in most of the reported cases and in the few cases which I have observed. The condition was originally described as a lesion resembling tuberculosis verrucosa cutis. I understand that the organism was not found in the sections. That is unusual. The organism is usually readily demonstrable in sections from early active lesions, although hard to find in those from older lesions.

DR. ANTHONY C. CIPOLLARO: I saw this patient for the first time last week. He was brought to the clinic by a physician who had been treating the condition for seven months, thinking it was a furuncle which was not responding to the usual topical remedies. Multiple sinuses give to the surface of the lesion a verrucous appearance. The periphery of the lesion is definitely infiltrated, making one suspicious of blastomycosis. Organisms were not found in the sections but were found on direct smears. A smear was taken from the pus expressed from the sinuses, and the organism of blastomycosis was found. Some organisms were seen to be in the budding stage. A biopsy specimen was taken from the edge of the lesion, and Dr. D. L. Satenstein, who examined the section, made a diagnosis of blastomycosis.

Psoriasis Vulgaris and Pustular Psoriasis. Presented by DR. ISADORE ROSEN.

F. A., a man aged 34, was first seen on May 3, 1937, when he presented a generalized eruption of twenty months' duration.

The eruption consists of variously sized erythematous, scaly and crusted patches, varying in size from that of a pinpoint to that of a silver dollar or even larger.

The scalp is involved. The soles show at the edge of the sharply defined patch some deep-seated vesicular lesions. The nails of the fingers and the toes show marked changes, consisting of grayish discoloration, lack of luster and, particularly on the toes, thick loosely attached white horny scales.

DISCUSSION

PROF. A. BUSCHKE, Berlin, Germany (by invitation): The appearance of this condition suggests to me the diagnosis of psoriasis arthropathica. When questioned, the patient said there was some arthritic involvement. I should like to mention the other type of eruption which sometimes so closely resembles psoriasis arthropathica, namely, keratosis blennorrhagica, which sometimes is due to a nonspecific cystitis, with no gonococcic infection. Considering these conditions side by side, one would feel that in psoriasis arthropathica one is not dealing with the usual causes of psoriasis, which are probably some endocrine disturbance and possibly focal infection. In the treatment of psoriasis arthropathica one cannot be satisfied with local care of the psoriasis and the arthritis, but it is necessary to use some endocrine preparation and to pay attention to the lipoid metabolism. I have had my best results with thyroid therapy.

A Case for Diagnosis (Dermatitis Venenata? Dermatitis Medicamentosa? Seborrheic Eczema?). Presented by DR. ABRAHAM WALZER, Brooklyn.

F. S., a woman aged 27, is presented because of an eruption on the face of two months' duration. The patient has never had any serious illnesses, and there have been no allergic diseases in her family. About three months ago the patient's baby, 22 months old, died of probable meningitis. Two weeks after that the patient became ill, complaining of various aches and pains. During this time she took several "feenamint" tablets and a few acetylsalicylic acid tablets. Shortly after this the eruption appeared on the face.

The patient was treated by several private physicians with local applications. She was finally hospitalized in a local institution, where she was treated with local applications and the internal administration of calcium gluconate, ephedrine and iron tablets. She was discharged from the hospital about two weeks ago, when the condition was practically the same as that present today. Patch tests with all her cosmetic preparations and tooth paste gave negative results.

Examination shows two large patches on the face, one involving both eyes, the forehead and the bridge of the nose and the other patch including both lips, the upper part of the chin and the nasolabial folds. The patches are separated by the normal skin of the cheeks and the lower half of the nose but are connected by thin strands of erythema running down both sides of the nose. They have fairly sharply outlined borders and are slightly infiltrated, somewhat elevated and dark red. The surfaces are dry and covered with a fine furfuraceous scale. On the cheeks and the upper part of the forehead are many scattered fine erythematous points. The upper and lower eyelids are edematous.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: This patient was under my observation at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for two weeks. I have never seen a skin so intolerant of any type of topical application as this patient's. It was necessary finally to resort to the use of cold solution of sodium chloride, which did benefit her. Emulsions and ointments seemed to aggravate the eruption. It is my impression that she gets a local irritation from fats. She says she notices that there is a recurrence starting on the lips and extending up the face whenever she drinks cream and eats butter; yet patch tests failed to show sensitivity. In this connection, I want to report a case of Dr. R. A. Cooke's, in which there developed around the eyelids a fixed eczematous eruption, which he proved to be due to the eating of tomatoes. The skin of a tomato applied to the face around the eyelids caused a relapse on several occasions. That is the first case, I think, in which a fixed eruption was proved to be due to

a food. Dr. Walzer's patient has simple vesicular dermatitis, maybe due to fats. There is no sign of lupus erythematosus or seborrheic eczema.

DR. ABRAHAM WALZER, Brooklyn: The history obtained from the patient, reported by Dr. Abramowitz, that the lesions are due to the ingestion of fats or are lighted up by such foods, might easily be obtained from many patients. When such a patient is exposed to the usual test of eating such foods, the results are usually negative. It is inconceivable that such lesions as this patient presents should be due to any type of food. Foods never cause such lesions and especially at these locations. In spite of the negative patch tests, I still think that the eruption is contact dermatitis or possibly seborrheic eczema made worse by the ingestion of some drugs or by the application of some external substance.

Fox-Fordyce Disease. Presented by DR. CHARLES WOLF.

M. M., a girl aged 15, has a widespread eruption in both axillae, consisting of chamois-colored discrete pinhead-sized polygonal papules. At the periphery of the areola of each breast there are several scratched papules. Itching is considerable. The eruption is intensified during the menstrual period. The condition has been present for about one year.

Psoriasis Generalisata. Presented by DR. CHARLES WOLF.

Morphea. Presented by DR. JESSE A. TOLMACH.

Idiopathic Macular Atróphy. Presented by DR. ABRAHAM WALZER, Brooklyn.

Sarcoid. Presented by DR. ISADORE ROSEN.

Lupus Erythematosus. Presented by DR. S. H. SILVERS, Brooklyn.

Hyperkeratotic Lichen Planus. Presented by DR. G. D. ASTRACHAN.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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May 21, 1937

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Kaposi's Sarcoma (Multiple Idiopathic Hemorrhagic Sarcoma). Presented by DR. DONALD M. PILLSBURY.

L. C., a well developed and moderately obese native-born American aged 48, had his right hand frostbitten five years ago. A short time later the hand assumed a violaceous color, which has persisted. During the winter the hand swells, but the swelling subsides during the summer. About two years ago he noted on the dorsum of the left hand a violaceous lesion, which has been slowly but progressively extending. For the past six months he has noticed similar discoloration on the third, the fourth and the big toe of the right foot and on the left ankle and for the past five weeks on the third and the fourth toe of the left foot. The entire right hand is involved with a dusky bluish brown blotchy plaque, and there is diffuse moderate swelling. On the ulnar side of the back of the left hand there is a sharply circumscribed raised plaque, the center of which is a striking red which varies in intensity, depending on interference with the circulation. On the third and the fourth toe of each foot and the big toe of the right foot there is a slightly violaceous raised and slightly infiltrated plaque. Two similar but somewhat more

brownish lesions are noted on the ankles, the outer side of the left ankle being particularly involved. The teeth are badly stained and carious. The tonsils are chronically infected. Examination of the heart reveals auricular fibrillation, but there is no other evidence of cardiac disease. Examination of the blood showed 5,000,000 red cells, 103 per cent hemoglobin, 7,000 white cells and a normal differential count. Urinalysis and the Kolmer and the Kahn test showed no abnormality. The electrocardiogram showed auricular fibrillation. Roentgenograms of the gastro-intestinal tract revealed no organic lesions. The sedimentation time was slightly above normal. Roentgenograms of the teeth showed no periapical infection. The lungs showed possible bronchiectasis at the bases, and there were increased density of the left ethmoid bone and thickening of the mucous membrane of the maxillary sinus. The basal metabolic rate was —5 per cent. The histologic picture was compatible with sarcoma of Kaposi. Treatment has consisted of local application of 75 roentgens of unfiltered roentgen radiation to each lesion once weekly. Five such treatments have produced marked improvement.

DISCUSSION

DR. FRANK C. KNOWLES: I think those who have observed cases of Kaposi's sarcoma would find considerable difficulty in making a clinical diagnosis in this case. There is usually a distinct mahogany color to the nodules. Here they are bluish brown, without the mahogany shade typical of Kaposi's sarcoma.

A Case for Diagnosis (Lichen Planus? Parapsoriasis?). Presented by DR. ARTHUR GOMERSALL PRATT, Camden, N. J. (by invitation) for DR. HENRY B. DECKER, Camden, N. J.

W. W., a white man aged 70, noticed nonpruritic papules varying in size from that of a pinhead to that of a pea on the abdomen about five weeks ago. No scales were present. In a few days similar lesions appeared in the sternal area and on the entire back, the extensor surfaces of the arms, the forearms and the legs. The sides of the face are somewhat similarly affected. The lesions are for the most part rather uniform slightly elevated flat-topped papules varying in color from dull red to violaceous. Many appear umbilicated. On the back especially they have a shiny brownish keratotic scale, which is easily removed. A certain amount of lichenoid shininess can be demonstrated on the purplish papules of the forearm and the hand. The lower lip shows a milky white change, which extends onto the buccal mucosa a trifle at the commissures; otherwise the oral mucosa is clear. The facial lesions are less elevated and distinct than those of other parts of the body. Mild itching is now present.

DISCUSSION

DR. W. O. ROOP, Atlantic City, N. J.: I am inclined to accept the diagnosis of lichen planus. It is true there is comparatively little itching, but I am inclined to base the diagnosis on the distribution of the lesions. The lesions on the wrist, I think, are more typical than the others.

DR. SIGMUND S. GREENBAUM: I agree with the diagnosis. The lesions on the mucosa of the lower lip, on the tongue and on the glans penis are characteristic.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: There is associated seborrhea, which gives the papules on the back a waxy appearance.

DR. VAUGHN C. GARNER: I was struck by the possibility that the lesions on the back might be those of early Darier's disease. There is an extensive profusion of discrete, closely crowded greasy papular lesions, rather typically distributed over the entire back.

A Case for Diagnosis (Schamberg's Progressive Pigmentary Dermatosis? Purpura Annularis Telangiectodes?). Presented by DR. S. R. KAUFMAN, Wilkes-Barre, Pa.

R. C., a white man aged 27, presents punctate hemorrhagic and telangiectatic lesions on the ankles, together with pigmentary deposits and some white, scarlike

areas. A purplish hue prevails in the majority of the lesions. No papular lesions have ever been observed. Eight years ago tiny purplish spots appeared on both ankles. They were not accompanied by itching. After about one week they disappeared, to recur every few weeks, gradually enlarging the region affected. The present outbreak began in November 1936, and the eruption has steadily progressed, involving the legs, the buttocks and the forearms. The Wassermann reaction is negative. Ultraviolet therapy produced marked improvement.

DISCUSSION

DR. FRANK C. KNOWLES: I do not think that this eruption resembles Schamberg's disease. Two different condition have to be considered: a recurring type of purpura and beginning angioma serpiginosum of Hutchinson. I think the patient has recurrent purpura. He states that he has chronic nephritis. He was examined several months ago for insurance and was rejected because of the condition of the urine. In all probability he has toxic purpura in which certain elements of the blood and the fibrinogen in particular have been altered.

DR. JOSEPH V. KLAUDER: I think the condition is purpura simplex.

Multiple Sarcoid of Boeck. Presented by DR. CARMEN CHRISTINE THOMAS, Wilmington, Del. (by invitation) for DR. JOHN H. STOKES.

E. G., a Negress aged 23, presents grouped erythematous fleshy nodules, varying in size from that of a pinhead to that of a hazelnut. They are grouped especially along the margins of the eyelids. The overlying skin is smooth and shiny. Oval lesions occur on the back and the sides of the trunk. The entire cutaneous surface is involved. There is generalized moderate nontender enlargement of all accessible lymph nodes. There is diffuse hyperplasia of the pharyngeal tissue. There is no involvement of the mucous membrane. In August 1936 scattered pea-sized psoriasiform lesions appeared on the face, the eyelids and the extremities and gradually covered the rest of the body. The patient was treated at another hospital for syphilis because of a positive Wassermann reaction. She received approximately twenty injections of neoarsphenamine intravenously. The lesions increased in number and size. Hoarseness began two months ago and has persisted. The Kahn and the Kline reaction are strongly positive. Sections from the skin of the upper part of the right arm showed tuberculous architecture, typical of sarcoid. Roentgen examination of the bones of the hands and the feet and of the long bones showed no abnormality; that of the chest revealed large, bilateral mediastinal masses at the hili. Treatment has consisted of two weekly injections of bismuth subsalicylate to date.

DISCUSSION

DR. SIGMUND S. GREENBAUM: This type of sarcoid is, I think, definitely tuberculous. It is the generalized nodular form described by Klauder and Weidman. None of the cases described by Kissmeyer in his book bear any resemblance to the case presented here or to those previously shown by me as instances of multiple benign sarcoid. The cases of sarcoidosis, as I prefer to call them, suggest a disease sui generis to me. There are too many factors in sarcoidosis which, in my opinion, conflict with the usually assumed tuberculous etiology.

DR. ABRAM STRAUSS: I agree with Dr. Greenbaum that the diagnosis is true tuberculosis rather than sarcoid of Boeck. I believe the roentgenograms show tuberculous involvement of the lungs.

A Case for Diagnosis (Reticulosis? Cutaneous Lipoid Dysfunction?). Presented by DR. THOMAS HUNTER STERNBERG (by invitation) for DR. JOHN H. STOKES.

F. B., a white woman aged 61, has had a papular eruption on the outer aspect of the right arm for four years. The eruption remained stationary up to a few months ago, since which time she believes a few new lesions have appeared. There has been no itching at any time. The papules are dull red; many of them are

flat and others conical. Diascopic pressure shows most of them to be pigmented. The patient has had diabetes for a number of years, controlled by diet. She does not take insulin. She has arrested pulmonary tuberculosis. Serologic tests of the blood gave negative results. The blood pressure was 115 systolic and 60 diastolic. The urine occasionally contained traces of sugar; the sugar content of the blood measured from 115 to 190 and the cholesterol content 402 mg. per hundred cubic centimeters. Sections showed localized collections of leukocytes in the upper part of the corium lying on a reticulum. Most of these were lymphocytes.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: The condition appears to me like possible lichen planus.

DR. SIGMUND S. GREENBAUM: My first impression was the same as that of Dr. Stokes—that the condition was an abortive type of lupus vulgaris—because under pressure the lesions certainly had some of the characteristics of ordinary lupomas.

DR. ABRAM STRAUSS: With the exception of the coloring, a great many of those lesions resemble closely verruca juvenilis plana. The color appears rather xanthomatous.

DR. FRANK C. KNOWLES: Why not a diagnosis of localized diabetic xanthoma? Two extremely interesting articles appeared in the last number of the ARCHIVES (Weidman, F. D.: Position of "Pseudodiabetic Xanthoma" Among the Lipoid Disturbances of the Skin [Urbach] ARCH. DERMAT. & SYPH. **35**:815 [May] 1937; Weidman, F. D., and Schaffer, H. W.: Xanthoma of the Skin and Larynx, ibid. **35**:767 [May] 1937) covering the subject of pseudodiabetic xanthoma. I suggest that this condition is a rather atypical form of diabetic xanthoma or pseudodiabetic xanthoma.

DR. JOSEPH V. KLAUDER: The lesion impressed me as being xanthomatous, in view of the fact that the patient has diabetes and a high cholesterol content of the blood.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. JOSEPH V. KLAUDER.

L. G., a white man aged 23, presents on the lower lip a crusting associated with a seropurulent discharge. The mucous membrane is exfoliated. The condition began in the latter part of February as an ulcer, gradually spread and now covers the entire lower lip. There has been no contact with chemicals. There is a scar on the left side of the face, the result of the destruction of a nevus. A smear from the lip showed many staphylococci. Dark field examination gave negative results. The blood count was within normal limits.

DISCUSSION

DR. W. O. ROOP, Atlantic City, N. J.: I suggest the diagnosis of seborrheic eczema of the lip. Recently I observed in one of the standard textbooks on dermatology a picture of which this eruption appears to be a counterpart. The diagnosis there given was seborrheic eczema of the lip, and I believe these conditions are now generally accepted as seborrheic types of eczema. Furthermore, there is definite seborrhea of this man's scalp, and I think this condition may well be considered seborrheic eczema of the lip.

DR. FRANK C. KNOWLES: Why not exfoliative cheilitis of the lip, with a superimposed infection?

DR. SIGMUND S. GREENBAUM: My impression—because of the history—is that this condition is a superficial form of cheilitis glandularis apostematosa and that in time this lesion, if it persists, may become the typcal form. The patient states that the entire condition disappeared completely six weeks ago, at which time a few lesions developed in the mouth. This is suggestive of a localized infection. I do not believe the condition is lupus erythematosus. I recall seeing a patient about four

or five years ago who had had a condition similar to the one shown here for a period of seven years, but that condition at no time disappeared. However, within a month the lesions cleared up under frequent alternate applications of 70 per cent alcohol and 1 per cent solution of iodine in alcohol.

Severe Acne, Probably Associated with Changes in the Central Nervous System. Presented by Dr. Donald M. Pillsbury.

E. H., a white woman aged 43, a patient of Dr. Edward Rose, in May 1921 had a severe fall down a flight of stairs. The menses ceased after the fall, and the following changes appeared in quick succession: (1) an increase in weight from 104 to 158 pounds (47.4 to 72 Kg.); (2) a marked increase in appetite; (3) a change in the contour of the face and the size of the feet; (4) severe headaches; (5) the appearance of severe acne of the face, and (6) dispositional changes (untidiness). The patient received a series of roentgen treatments for the acne and later for hirsuties, the latter treatment being applied at a nonmedical establishment. The scars of a face-lifting operation are present about the ears. There is rather marked rosaceiform flushing of the face, accompanied with seborrheic oiliness of the upper part, pigmentation and atrophy of the cheeks and the chin, and scars of old acne. Medical examination revealed hirsuties of the trunk, areolar pigmentation and enlargement of the vulva. Exhaustive laboratory studies have been made, including determination of the basal metabolic rates, many types of chemical study of the blood, roentgenograms of the skeleton and the head, a urogram and perinephric injections of air. The only abnormal findings were a basal metabolic rate of —14 per cent, a slightly elevated blood cholesterol content and some impairment of dextrose tolerance. The only treatment has been administration of dilute hydrochloric acid by mouth and continued application of a cosmetic preparation to hide the deformity.

DISCUSSION

Dr. Robert L. Gilman: How long ago was the roentgen treatment given?

Dr. Abram Strauss: She had, according to her story, two courses of roentgen treatment, one for acne, during which she got a slight burn, and one at one of these medical institutes for the removal of hair, during which she got another burn. Then she went to have a mole removed and instead of treating that, the operator performed a face-lifting procedure, from which the patient got the scar.

Morphea. Presented by Dr. Elmer R. Gross, Wilmington, Del. (associate member).

E. C., a girl aged 5 years, was presented in the fall of 1936 at a meeting of the Philadelphia Dermatological Society, because of four sharply circumscribed patches of morphea on the left forearm. She is now presented to show the striking improvement following the oral administration of 10 grains (0.6 Gm.) of ammonium chloride three times a day and ingestion of a high ketogenic diet. The areas are definitely softer; there has been no progression of the lesions, and the texture and the color of the overlying skin are approaching normal.

DISCUSSION

Dr. Vaughn C. Garner: A little girl under my care has been taking ammonium chloride for six months, and there is no doubt that the patches have undergone involution, but the question is, would they have done so without it?

A Case for Diagnosis (Extensive Pigmentation). Presented by Dr. Abram Strauss.

I. L., a white youth aged 19, presents thousands of pigmented spots, which have not varied to any extent. Exposure to the sun only causes the pigment to become slightly darker. The patient was born with the condition, and treatment has not altered it in any way.

DISCUSSION

Dr. Joseph V. Klauder: I should suggest that the urine be examined for melanin. I think in similar cases of pigmentary nevus melanin has been reported

in the urine. I suggest further that the eyegrounds be examined for pigmentary changes and the family history be looked into for any familial tendency. How many of the relatives are freckled?

DR. FRANK C. KNOWLES: I have observed a case somewhat like this in an Italian family, but in that case there was a dark-skinned ancestor in the background. One would think there was something in the antecedents somewhere that would give rise to these curious pigmentary changes in the skin of this patient. It might be wise to go thoroughly into his background. There is certainly more than a suspicion that there has been some dark-skinned ancestors in the line, whose strain is now coming to the fore.

DR. ABRAM STRAUSS: The family history, so far as I can determine, gives no indication of such a heritage. The mother is white skinned, as are the sister and the father. The remarkable thing to me when I saw the patient was not the pigmentary phenomenon but the peculiar appearance of this boy's face—almost a Negroid physiognomy. It struck me that he was one of those throwbacks from the present into the anthropoid age; his expression, the slope of his forehead, the lips, the nose and the recession of the eyes almost reminded me of Neanderthal man. I cannot get any history of intermixture of races. Of course, that is a pretty delicate matter to discuss. I have already written, describing the case, to Dr. Aleš Hrdlička, Washington, D. C., to see what comment he might make.

DR. ROBERT L. GILMAN: I think this case is peculiar. I had the same thoughts Dr. Strauss did because of the cast of the patient's physiognomy, but I believe that geneticists hold that Negroid features and pigmentation are bound to be recessive. It is most unusual to have these characteristics come out as a dominant strain. In other words, they are absorbed and do not tend to recur.

DR. THOMAS BUTTERWORTH, Reading, Pa.: In addition to the dark spots, this boy has several large brown patches similar to the coffee-colored lesions in Recklinghausen's disease.

DR. B. L. KAHN: In the last case of Recklinghausen's disease which I presented here the condition appeared practically at birth, its first manifestation being a nevus on the scalp, which I removed when the child was 3 weeks old. Shortly afterward various pigmentary lesions appeared on the chest and on the forearms. Today the child is 6 years old and has typical Recklinghausen's disease dating back practically to birth.

A Case for Diagnosis (Pigmentation of the Ankles and the Eyelids). Presented by DR. J. P. GUEQUIERRE.

A. B., a white man aged 37, injured his left ankle fourteen years ago. Pigmentation appeared in that area several years later. Five years later similar pigmentation appeared on the right ankle without any preceding trauma. During the past year pigmentation of a lighter reddish-yellowish hue has appeared on the lids of both eyes at the same time. There are no symptoms, and no possible pigmentation-producing foods have been taken in excess.

DISCUSSION

DR. JOSEPH V. KLAUDER: I thought of the possibility of pigmentation following extravasation of blood. I do not favor the diagnosis of Schamberg's disease.

DR. ROBERT L. GILMAN: I saw this patient by daylight, and I thought the pigmentation, particularly about the eyes, resembled localized carotene pigmentation rather than any condition produced by melanin. Dr. Guequierre went into the dietary history carefully, however, and there was nothing to suggest any carotene element.

DR. J. P. GUEQUIERRE: The patient said he did not like carrots and had not eaten them in years.

Essential Shrinking of the Conjunctiva (Pemphigus of the Conjunctiva). Presented by DR. JOSEPH V. KLAUDER.

C. C., a white man aged 57, of good general health, complains of impaired vision. The left cornea is smaller than the right and is partly opaque and lusterless. The conjunctiva over the bulb appears to be stretched and dry, and there is shriveling of the palpebral conjunctiva. There is no adhesion of the palpebral to the bulbar conjunctiva. The cornea and the conjunctiva of the right eye are normal. Examination of other mucous surfaces showed no abnormality.

DISCUSSION

DR. SIGMUND S. GREENBAUM: This case brings up the question whether essential shrinkage of the conjunctiva, as determined by the ophthalmologist, is the same condition as that which dermatologists term pemphigus vulgaris. Either there is a separate disease involving the conjunctiva and followed by atrophy and cicatrization or there is pemphigus vulgaris limited to the mucous membrane of the eye. I have given this subject a good deal of thought over a period of years, and in one of my own cases the lesions were first limited to the conjunctiva, subsequently spread to the mucous membrane of the mouth and later became generalized as typical pemphigus vulgaris. Hence, the condition is perhaps a localized form of what is called pemphigus vulgaris, limited to the mucous membranes of the eye.

DR. JOSEPH V. KLAUDER: I do not believe the two diseases are related. I am unable to discover the origin of the term pemphigus of the conjunctiva. I think the desirable name for the disease is "essential shrinking of the conjunctiva" and not "pemphigus of the conjunctiva." In some cases of pemphigus vulgaris blebs have appeared on the conjunctiva. I have never seen that manifestation, but in endeavoring to trace the origin of the term "pemphigus of the conjunctiva," I have noted that confusion arose from the appearance of blebs on the conjunctiva in patients with pemphigus vulgaris. The end-results of such blebs simulate essential shrinking of the conjunctiva. I think that is possibly the basis for the confusion of terms. In many cases there is shriveling of all mucous surfaces, including the urethra, the anus and the vagina. This does not occur in pemphigus vulgaris. It does not appear in this case. I believe there is a relation between essential shrinking of the conjunctiva and what is known as balanitis xerotica. In this disease there is shriveling of the mucous membrane of the urethra. There is therefore a clinical relation between these two diseases. It is possible that balanitis xerotica is simply a localized form of the disease called essential shrinking of the conjunctiva. The treatment of essential shrinking of the conjunctiva is unsatisfactory. I am under the impression that the condition occurs more frequently in those born in the East. It is a rare disease; the series of cases at the Wills Hospital has not been large, but there has been only one American-born patient out of the four or five patients with this disease whom I have seen in the past ten years.

DR. SIGMUND S. GREENBAUM: I have observed several cases like this one. Of two of them that come to my mind, one was that of a Jewess who had involvement of both conjunctivae; the other was that of a gentile born in the United States. She had involvement of the oral mucosa, with atrophy following what appeared to be a bullous condition and involvement of one of the eyes. Both patients subsequently died, but I do not think they died of this condition.

Mild Course of Untreated Interstitial Keratitis in Brother and Sister; Discussion of Syphilitic Uveitis. Presented by DR. JOSEPH V. KLAUDER.

These patients, M. and J. G., are brother and sister. The girl is 16 years old, the boy 14. The girl had "sore eyes" at the age of 7 years. No antisyphilitic treatment was administered. She was first seen by me in March 1937. Six months prior to that time the right eye became inflamed, and five months later the left eye became inflamed. When she was first seen the inflammation of both eyes was quiescent; there were opacities in both corneas. Slit lamp examination of both eyes showed the cornea to be generally hazy throughout and densely infil-

trated in the lower portion. There were numerous blood vessels throughout its entire thickness, mostly superficial, but many deep. There were many white, muttonlike keratotic precipitates. Excrescences of the epithelial layer of pigment could be seen. These were probably adherent to the lens. The slit lamp diagnosis was old interstitial keratitis and uveitis. The vision was, right eye 6/21, with correction 6/15; left eye, 6/60, with correction, 6/60.

The boy was first seen by me in March 1937. He had untreated bilateral interstitial keratitis of about three months' duration. The right cornea was opaque at the center, and there was no inflammation. The left cornea was entirely opaque, but there was no inflammation. The vision of the right eye was limited to perception of movements of the hand at 1 foot (40 cm.); that of the left eye was 1/60. One injection of 100 mg. of a bismuth preparation was given. The boy did not return to the clinic until May 17. At this time examination showed remarkable clearing of both corneas, only faint opacities being present in the center of each cornea. The vision was, right eye 4/60, with correction 6/15; left eye, 6/30, with correction, 6/30.

DISCUSSION

DR. JOSEPH V. KLAUDER: There are some interesting points about these two patients. Regarding the girl, clinically the condition of her eyes is quiescent; there is no inflammation. Slit lamp examination discloses, in addition to deep blood vessels in the cornea that characterize old interstitial keratitis, many characteristic deposits of uveitis on Descemet's membrane. Uveitis could not be diagnosed with certitude without the aid of the slit lamp examination. This examination is of considerable importance to a proper study of interstitial keratitis and other ocular diseases. Is the uveitis syphilitic? It apparently is not part of the interstitial keratitis, which is inactive. Its syphilitic origin is presumptive. I believe that statement applies to all cases of uveitis unless associated with active interstitial keratitis or with iritis in patients with secondary or late secondary manifestations of syphilis. If such an association is not present, I am not sure that syphilis is a factor in what is clinically called uveitis. Response to antisyphilitic treatment in such patients, in my observations at the Wills Hospital, justifies this statement.

The vision in the girl's left eye and the boy's right eye was definitely improved by refraction. The final vision in patients with interstitial keratitis should always be determined by refraction. Final vision without refraction is not accurate, since many patients with old interstitial keratitis have astigmatism and myopia.

The boy furnishes an example of how severe interstitial keratitis can eventuate favorably in the absence of treatment. Cases like these, not at all uncommon, make it difficult to draw conclusions concerning the efficacy of antisyphilitic treatment in interstitial keratitis.

MINNESOTA DERMATOLOGICAL SOCIETY

ANDREW M. DAVIDSON, M.D., *Presiding*

Winnipeg, Canada, June 27, 1937

F. W. LYNCH, M.D., *Secretary*

Lichen Planus of the Penis. Presented by DR. ANDREW M. DAVIDSON, Winnipeg, Canada (associate member).

F. R., a single man aged 25, a Canadian shipper, presents serpiginous lesions on the glans penis of eight months' duration. The outline has varied during the period, but there is a tendency for the lesions to enlarge.

The blood and the urine were normal; the Wassermann reaction was negative, and the physical examination showed no abnormality.

The patient exhibits a condition on the tongue simulating lichen planus.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: There is a great similarity clinically between lichen planus of the mucous membranes of the mouth and so-called submucous thrush. My associates and I have recently been studying a group of cases of these conditions from the clinical, the laboratory and the pathologic standpoint. One of the cases presented today clinically could be one of submucous thrush; the others, including the one under discussion, were typical instances of that disorder.

DR. S. E. SWEITZER, Minneapolis: Roentgen therapy to the spine sometimes has a good effect on such lesions, a dose of ½ or ¾ skin unit of filtered radiation once in three or four weeks being sufficient.

Pemphigus of the Mouth. Presented by DR. ANDREW M. DAVIDSON, Winnipeg, Canada (associate member).

Miss M. W., aged 33, a Canadian bookkeeper, presents a bullous eruption of the mouth and the throat, which has been constantly present for seven years. The bullae arise on an apparently normal mucous membrane, are about 1 cm. in diameter and contain clear fluid. They are painful and are a source of great discomfort, because the patient wears dentures. After rupture of the bullae a raw bleeding surface remains.

The physical examination showed no abnormality. Results of Pels-Macht phytopharmacologic tests on ten determinations varied from 43 to 63 per cent. The condition has proved resistant to all forms of treatment.

Bullous Eruption of the Mouth. Presented by DR. ANDREW M. DAVIDSON, Winnipeg, Canada (associate member).

Mrs. G., a housewife aged 59, of Scotch and French descent, presents a bullous eruption of the mouth, accompanied with leukoplakia of both buccal mucous membranes, of five years' duration. She is edentulous. This condition originated during a severe attack of arsenical dermatitis, arsphenamine having been used in the treatment of trench mouth. The condition has never entirely cleared during this time and has resisted all forms of treatment. The Pels-Macht phytopharmacologic test gave a result of 75 per cent; the Wassermann reaction was negative, and the physical examination showed no abnormality.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I think the condition is due to the old-fashioned dental plates.

DR. CARL LAYMON, Minneapolis: It has not been my experience that pemphigus originating on the mucosa is more rapidly fatal than that affecting only the skin. In fact, several patients under my observation in Minneapolis, who have had bullous lesions in the mouth considered as pemphigus, have experienced a rather mild course, being free from constitutional symptoms for several years.

Lupus Erythematosus Disseminatus Subacutus. Presented by DR. W. GEORGE BROCK, Winnipeg, Canada (associate member).

D. B., a Jewess aged 27, first noticed an eruption in January 1933. Examination in 1935 showed diffuse partial alopecia. The scalp was scaly. An eruption on the face, the neck and the back was regarded as the lupus pernio type of lupus erythematosus. There were small discrete atrophic scars on the interphalangeal joints, surrounded by telangiectatic haloes. Similar lesions were present on the vertebral column in the middorsal region. The finger-tips were blue, and long graceful capillary loops were plainly visible through the epidermis. Pains in the muscles and the joints had been present for one year; they were not relieved by the removal of infected teeth.

Roentgen studies of the chest showed no abnormality. The Kline and the Kahn test were weakly positive. A study of the blood showed 60 per cent hemo-

globin, 3,440,000 red blood cells and 4,170 white cells. The temperature varied from 99 to 101 F.

At present the hair has grown in thickly over the whole scalp, the new hairs being several inches long and strong. All traces of pigmentation have left the face. The epidermis is smooth and soft. There is a faint macular atrophy on the cheeks, which is more pronounced in the submental region. These areas are a delicate pink. Only the atrophic scars remain over the joints of the fingers. The circulation has become normal in the finger-tips.

Lupus Vulgaris of the Neck. Presented by Dr. W. George Brock, Winnipeg, Canada (associate member).

Miss M. G., a Greek girl aged 21, born in Winnipeg, states that the glands of the left side of the neck became enlarged in 1928. Two years later they were excised as tuberculous glands. A sinus persisted at the angle of the left mandible. A small brown nodule appeared at the margin of the sinus. In November 1930, when I was consulted, there were four large oval areas of typical lupus vulgaris occupying the entire left submaxillary region and the anterior triangle of the left side of the neck. The elementary lesion was a soft brownish nodule presenting typical apple jelly appearance with the diascope. A biopsy was done, and sections showed typical "tubercles" throughout the cutis.

In February 1937 the entire area of involved skin was excised by surgical diathermy. Later a full thickness cutaneous graft was done. At present there are about ten small soft elevated reddish brown nodules, distributed singly at intervals in the healed wound about the graft.

DISCUSSION

Dr. H. E. Michelson, Minneapolis: The treatment of lupus vulgaris is a tremendous problem. The members may know that Germany is making a national fight against the disease, and I think they are agreed that the salt-free diet is of great value. For my own part, I have not had enough experience with excision to call it a treatment of choice. One does not know how much to excise, and the scarring is sometimes disfiguring. The thing one must not forget is that the patient has tuberculosis, and that treatment of the tuberculosis is important.

Dr. S. E. Sweitzer, Minneapolis: I suggest the use of mercuric nitrate for lesions on the mucous membrane.

Lupus Erythematosus of the Face. Presented by Dr. Andrew M. Davidson, Winnipeg, Canada (associate member).

W. H., a single man aged 23, Swedish, a theater doorman, presents lupus erythematosus of the face, affecting both cheeks, the ears and the forehead, of three years' duration. Physical examination showed no other abnormality. The tuberculin test gave negative results; roentgenograms of the chest were clear. The Wassermann reaction was negative. The patient's father and mother and seven brothers and sisters are alive and well.

The patient was treated with sodium thiosulfate and quinine bisulfate, and the condition responded to injections of solganol (the disodium salt of 4-sulfomethylamino-2-auromercaptobenzene-1-sulfonic acid).

DISCUSSION

Dr. F. W. Lynch, St. Paul: What was the dosage of quinine used in this case?

Dr. Andrew M. Davidson, Winnipeg, Canada (associate member): Quinine bisulfate, 5 grains (0.32 Gm.), three times a day for three months.

Dr. Hamilton Montgomery, Rochester, Minn.: It is difficult to explain the prevalence of lupus erythematosus in this part of the country on the basis of light alone. Certainly in Minnesota and in Winnipeg there is a great deal more lupus

erythematosus than is seen, for instance, in Boston on the one hand and in southern cities on the other. Hence, there must be factors besides light. W. F. Petersen has written four volumes on "The Patient and the Weather" (Ann Arbor, Mich., Edwards Brothers, Inc., 1936). Dr. Russell Wilder recently informed me that the death rate from diabetes was thirty deaths per hundred thousand in the northwest, but only twelve per hundred thousand in Ohio. McCoy has recently emphasized that leprosy is endemic in the gulf states but dies out in the northern states, Minnesota being an outstanding example of the latter fact. I hope Dr. Davidson will go further in the correlation of weather and barometric readings in his studies on lupus erythematosus.

A Case for Diagnosis (Schamberg's Disease?). Presented by Dr. Andrew M. Davidson, Winnipeg, Canada (associate member).

Miss I. K., aged 53, a Canadian bookkeeper, presents symmetrical telangiectasia of the lower limbs. The lesions are the size of a pinhead and resemble cayenne pepper. There have been no subsequent symptoms, and the patient thinks the lesions have been caused by using beauty maid hair remover, which appears to be a fine emery paper.

DISCUSSION

Dr. H. E. Michelson, Minneapolis: I think the discussion of Schamberg's disease is much ado about nothing. I do not think it should be called a disease. It is merely an accompaniment of altered circulation, and whether there is one type of blood pigment or another does not alter the condition a great deal. To me the condition is merely a topic for amusing but valueless discussion.

Radiodermatitis of the Hands. Presented by Dr. Andrew M. Davidson, Winnipeg, Canada (associate member).

W. O. S., a married man aged 40, a Scotch optician, exhibits radiodermatitis with telangiectasia and keratoses and brittle nails with longitudinal ridging. The ring finger of the left hand was amputated in 1932. In 1934 the index, the middle and the ring finger of the right hand were amputated.

The patient had been treated by roentgen irradiation for weeping eczema of the hands for five years.

The physical examination showed nothing relevant.

DISCUSSION

Dr. John Butler, Minneapolis: The patient has one finger that should be amputated now.

Dr. Hamilton Montgomery, Rochester, Minn.: The prognosis in this case is grave. There was no glandular involvement when the patient was in Rochester, Minn. Specimens for biopsy at different times have revealed grade 2 and grade 4 epithelioma. Dr. Thomas Saunders has recently reviewed a group of 259 cases of chronic radiodermatitis which were observed at the Mayo Clinic between the years 1930 and 1934. In those cases in which chronic ulceration, keratoses and malignant changes develop, complete removal by cauterization, excision or amputation of the digit or extremity should be performed. To temporize results in further trouble. Small keratoses should be thoroughly cauterized. A lesion showing epitheliomatous change should be completely excised. As a rule, the larger the epitheliomatous ulcer, the higher the degree of malignancy; but at times a small ulcer may be highly malignant histopathologically.

Dr. H. E. Michelson, Minneapolis: Many cases of chronic radiodermatitis occur in physicians. I think it is important to put patients with this condition on a routine, keep the hands soft and treat the keratoses as they appear. Impressing the patient with the great need for daily care is important and unquestionably is a great aid in preventing severe sequelae.

Dermatitis Factitia: Ulcers of the Leg. Presented by Dr. W. George Brock, Winnipeg, Canada (associate member).

Mrs. C., an Englishwoman, aged 60, suffered an injury to the thumb two years after her arrival in Canada twenty-five years ago. Resulting lymphadenitis persisted until incision of the node nine years ago. Similar nodules appeared in the supraclavicular areas eighteen years ago and have drained and healed many times. Bluish red nodules developed on the legs each winter, ulcerated, drained and healed, with pigmented scarring of linear and geometric arrangement. Erysipelas of the right thigh and leg five weeks ago was followed by the present eruption.

Repeated bacteriologic cultures from the ulcers showed only Staphylococcus aureus. The Wassermann reaction was negative. Urinalysis showed no abnormality. Examination of the blood showed 60 per cent hemoglobin, 5,030,000 red cells, and 7,150 white cells.

Microscopic sections from two specimens showed chronic inflammation with giant cells of the foreign body type (a few were suggestive of the Langerhans type) and an ulcer with a necrotic base and numerous pus cells.

At this time the right leg, knee and thigh are swollen. The enlargement is symmetrical. There is no pitting on pressure. The tissues feel hard. On the midportion of the posterior aspect of the right thigh is a group of five ulcers. Six more are distributed irregularly over the surface of the leg. The ulcers are from ¼ to ⅜ inch (0.6 to 1 cm.) in diameter. The borders of the ulcers are slightly elevated, regular, rounded and dull red. The bases are obscured by tenacious yellow seropurulent matter. There are a scar in the right axilla and one superior to each sternoclavicular joint. Numerous ones are present on each leg. They vary in size from ½ to 1½ inches (1.3 to 3.8 cm.) in diameter. They are smooth, vary in shape from round to octagonal and are surrounded by a zone of hyperpigmentation. The scars on the lower part of the left leg are arranged geometrically. On the outer aspect there are four in a line, three in a parallel line and others in geometric relation to these.

DISCUSSION

Dr. John Butler, Minneapolis: The fact that this woman shows these bizarre lesions so willingly is a point in favor of a diagnosis of factitious dermatitis.

Dr. H. E. Michelson, Minneapolis: I approve of Dr. Brock's approach and view of this case. It is surprising how many tyrants of this sort sit on the throne in some small home and rule the hard-working members of the family. If they are unable to rule by one means they do so by another, and in this case pity is stimulated or elicited by the lesions of the skin.

Seborrheic Eczema. Presented by Dr. W. George Brock, Winnipeg, Canada (associate member).

Bullous Eruption of the Mouth. Presented by Dr. Andrew M. Davidson, Winnipeg, Canada (associate member).

Lichen Planus Confined to the Mouth. Presented by Dr. Andrew M. Davidson.

Leukoplakia of the Mouth. Presented by Dr. Andrew M. Davidson.

Lupus Vulgaris of the Forehead. Presented by Dr. Andrew M. Davidson.

Lupus Vulgaris of the Left Cheek and the Ears. Presented by Dr. Andrew M. Davidson.

Lupus Vulgaris of the Neck. Presented by Dr. Andrew M. Davidson.

Recklinghausen's Disease. Presented by Dr. Andrew M. Davidson.

Rodent Ulcer. Presented by Dr. Andrew M. Davidson.

A Case for Diagnosis. Presented by Dr. Andrew M. Davidson.

Dermatitis Herpetiformis. Presented by Dr. Andrew M. Davidson.

Dermatitis Medicamentosa. Presented by Dr. Andrew M. Davidson.

Lupus Vulgaris of the Neck. Presented by Dr. Andrew M. Davidson.

Rodent Ulcer of the Nose. Presented by Dr. E. J. Washington, Winnipeg, Canada (associate member).

Keloid of the Bridge of the Nose. Presented by Dr. E. J. Washington.

Book Reviews

Lehrbuch und Atlas der Haut- und Geschlechtskrankheiten. By Dr. Karl Zieler, ö.o. Professor und Vorstand der Universitäts-Klinik und Poliklinik für Haut und Geschlechtskrankheiten in Würzburg, Germany. Fourth edition. Cloth. Price, 56 marks. In two volumes. Text, 684 pp., with 171 illustrations; atlas, 196 plates, with 378 colored illustrations. Berlin and Vienna: Urban & Schwarzenberg, 1937.

The work of Zieler consists of two volumes, one an atlas and the other an illustrated textbook. The atlas contains 378 colored illustrations, many of which are from Jacobi's atlas. They are well chosen and most beautifully reproduced. In this fourth edition there are 38 new colored illustrations. The volume containing the text has 130 black and white drawings of histologic slides by Freytag, which constitute perhaps the most valuable feature of the book. To syphilis are devoted 179 pages, and to gonorrhea, 70 pages. Ulcus molle is adequately described, although lymphogranuloma venereum is allotted only 2 pages. The new edition contains new material on the physiologic characteristics of the skin and on allergy, eczema, toxicoderma (especially occupational disease), purpura and fungous infections of the skin. A revision has been made of some of the sections on syphilis, and an excellent discussion on immunity, on syphilis of special organs and on the by-effects of arsphenamine therapy is included. The text has been written in language which is clear and easily understood. A moderate number of authors are mentioned by name, although bibliographic references are omitted.

Minor criticisms may be made of certain things, which include some unusual features in classification. In chapter 17 the author groups diseases due to protozoa with those of unknown etiology. In the same chapter he includes erythema nodosum, many causes of which are known. In the chapter on fungous diseases he includes pityriasis rosea, though fungous causation for that disease is merely speculative. In the chapter on pruritic diseases are included pemphigus vulgaris as well as the foliaceous and vegetating types. The author speaks of severe itching as a definite feature of pemphigus vulgaris, which is contrary to the usual experience. He devotes one paragraph to lichen ruber acuminatus and states that he does not consider this to have been established as the same as pityriasis rubra pilaris. There is no uniformity in nomenclature, the names of some diseases with well known Latin names having been given German titles.

With regard to size this work stands between the small book for students and the comprehensive single textbook. The work of the printer is excellent, the type being extremely legible and the black and white illustrations unusually clear. The heavy glazed paper which has been used unfortunately makes the book extremely heavy. The two volumes, and particularly the atlas, are valuable additions to the library of any physician interested in dermatology.

News and Comment

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

The American Academy of Dermatology and Syphilology was formally inaugurated on Jan. 14 and 15, 1938, in Detroit. More than three hundred dermatologists were present at the meeting. The large attendance was made possible by the cooperation of the Central States Dermatological Association, the Mississippi Valley Dermatological Society and the Chicago Dermatological Society.

The constitution which was adopted allows reputable dermatologists who have had at least three years of practice, teaching experience or training in dermatology and syphilology to become fellows. After Jan. 1, 1940, certification by the American Board of Dermatology and Syphilology will be a requisite for fellowship. Those who fail to be certified will be eligible for associate membership.

Provision was made for a class of junior members, which will include those in training to become dermatologists and syphilologists. They will not have the privilege of voting or of serving as officers, directors or members of committees and will be exempt from the payment of dues and assessments. On completion of their training they will, after Jan. 1, 1940, be eligible to become associates.

Every effort was made to make the academy as democratic as possible. Thus, there was included in the constitution a provision requiring the nominating committee to present two names for every office, in addition to maintaining the usual privilege of nomination from the floor. Provision was made to prevent the continuance in office of any group of men by the stipulation that no director should continue in office for more than six consecutive years.

The educational features of the meeting consisted of lectures and demonstrations relating to syphilology, mycology, histopathology and allergy by teachers who are leaders in their respective fields. That the efforts of the speakers were appreciated was shown by the good attendance, the only criticism to be heard being that it was impossible to be in three rooms at the same time. The educational program will doubtless be lengthened at future meetings, and other features, such as formal papers and published transactions, will receive due attention. A large clinic was held in the Harper Hospital by the dermatologists of Detroit.

The social aspect of the gathering was favored by the fact that all the meetings (except the clinic) were held in one large hotel, where most of the members had reservations. A banquet was held, at which over two hundred members were present, the entertainment being provided by Detroit dermatologists.

The following officers were elected: president, Dr. Howard Fox, New York; vice president, Dr. Paul A. O'Leary, Rochester, Minn.; secretary, Dr. Earl D. Osborne, Buffalo; treasurer, Dr. Clyde L. Cummer, Cleveland.

The following men were elected members of the board of directors: Drs. Samuel Ayres, Los Angeles; Samuel W. Becker, Chicago; Theodore Cornbleet, Chicago; Clyde L. Cummer, Cleveland; Clark W. Finnerud, Chicago; Howard Fox, New York; Harther L. Keim, Detroit; Joseph V. Klauder, Philadelphia; Frank C. Knowles, Philadelphia; Everett S. Lain, Oklahoma City; H. E. Michelson, Minneapolis; Paul A. O'Leary, Rochester, Minn.; Earl D. Osborne, Buffalo; Marion B. Sulzberger, New York, and Martin T. Van Studdiford, New Orleans.

It is planned to have the next meeting of the academy in St. Louis in November 1938, immediately preceding the convention of the Southern Medical Association in Oklahoma City.

Application blanks will soon be sent to all dermatologists in the United States and Canada. Those not receiving them are requested to communicate with the secretary, Dr. Earl D. Osborne, 471 Delaware Avenue, Buffalo, N. Y.

DEATHS

Dr. C. Morton Smith, of Boston, died suddenly on Saturday, Jan. 8, 1938.